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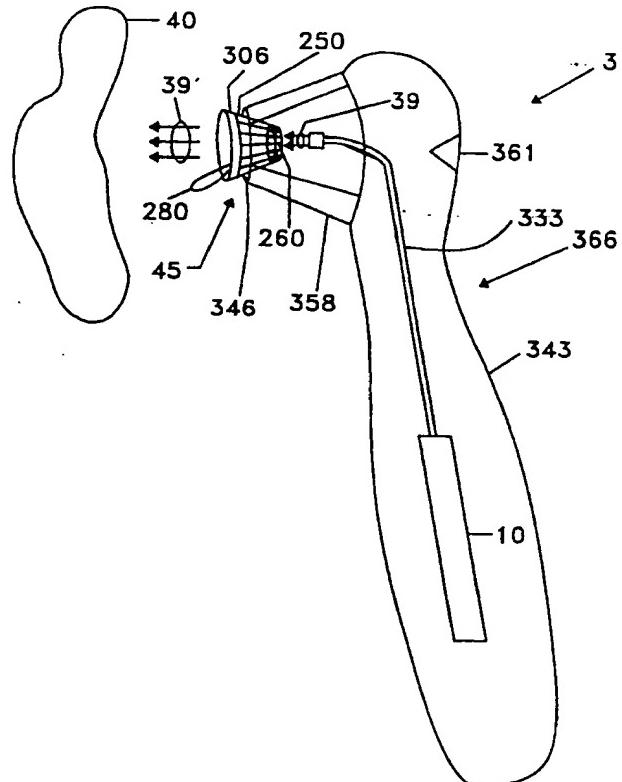
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(54) Title: ANALYZING SYSTEM WITH DISPOSABLE CALIBRATION DEVICE

(57) Abstract

A system and method for calibrating a measurement instrument (3) prior to making a measurement on a material or tissue (40) includes utilizing a removable calibration device (45) to calibrate the instrument, then removing a target portion of the calibration device so that a measurement may be performed. The target portion of the calibration device may have reflective/scattering properties, transmissive properties, or fluorescent properties that are used by the instrument to perform a calibration operation. A method embodying the invention may include making a bilirubin concentration measurement on a skin of a patient by measuring the amplitude of light reflected from the patient's skin at first, and second wavelengths indicative of a blood content of the patient's skin; measuring the amplitude of reflected light at a third wavelength indicative of an uncorrected bilirubin concentration; and then calculating a corrected bilirubin concentration based on the three measurements.



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ANALYZING SYSTEM WITH DISPOSABLE CALIBRATION DEVICE**BACKGROUND OF THE INVENTION****1. Field of the Invention**

This invention relates to instruments that measure characteristics and/or conditions of target materials or tissues, and in particular, to such instruments that utilize a calibration device. The invention also relates to apparatus and methods of determining a patient bilirubin concentration.

2. Background of the Related Art

There are a variety of measuring instruments that utilize light to detect physical characteristics or conditions of a material. Some such instruments are used by medical personnel to determine a condition of a patient. The use of light to determine a characteristic or condition of a target material is generally called spectroscopy. Spectroscopy has become more common in medical applications with the development of appropriate and inexpensive light sources, detection devices and optical fibers that allow for minimal invasiveness.

Typically, spectral reflectance, scattering, transmittance, fluorescence (normal and time resolved) and Raman spectroscopy are used to evaluate materials in order to determine the types of materials present and to measure their concentrations.

One type of spectroscopy, reflectance spectroscopy, involves diffusely reflecting light from a target material, and analyzing the reflected light. In another type of spectroscopy, called transmittance spectroscopy, light passes through a target material, and the transmitted light is analyzed. In other spectroscopic methods, illuminating a target material may cause the target material to emit fluorescent or luminescent light that can then be analyzed. In still other spectroscopic methods, a target material may be illuminated with polarized light, and reflected or transmitted light is analyzed to determine how the polarization of the light has changed. The polarization change can be used to determine characteristics or conditions of the target material.

An example of a spectroscopic measuring instrument is shown in Figure 3C. The instrument 3 emits light, at one or more wavelengths, from a nose portion. Light that is scattered or reflected from a target material 40, or light generated by the target material, is then collected and analyzed by the instrument to determine a characteristic or condition of the target material 40.

Spectroscopic instrument accuracy can be affected by variations in light source intensity, spectral characteristics, lens-aging, lens cleanliness, temperature, detector sensitivity changes, and electronic drifting. To correct for any potential measuring inaccuracies, it is common to periodically calibrate a spectroscopic measuring instrument. Calibration techniques usually involve conducting a measurement on a test target having characteristics that remain stable over time and over a range of

temperatures. The calibration techniques can be used to compensate for instrument to instrument variations, and for any changes that an individual instrument may experience over its working lifetime.

During a calibration operation, a spectroscopic measuring instrument is aimed at a calibration target having known optical properties. Light is then scattered or reflected by the calibration target, and received back in the instrument. Because the calibration target has known optical properties, the instrument is able to perform a calibration operation to ensure that the instrument continues to deliver accurate results.

Also, some measuring instruments may use a reference target as part of a measurement process. In such a device, the instrument is aimed at a reference target having known optical properties. Light from the instrument is scattered or reflected from the reference target, and a reading is taken. The results of the measurement operation conducted on the reference target can then be used as a standard or reference against which patient measurements are judged. For instance, the result of a patient reading could be derived by determining a difference or ratio between a patient reading and a reading taken on a reference target. Because the optical properties of the reference target are known, variations in light output or detector sensitivity can be accounted for by use of the reference target.

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Throughout the remainder of the application, including the claims, the terms "calibration target" and "reference target" are used interchangeably. Any reference to a calibration target is equally applicable to a reference target, and vice versa.

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When a measuring instrument is used with human or animal patients, steps must be taken to ensure that use of the instrument does not contaminate or infect the patient. When the instrument is successively used to examine two different patients, steps must be taken to ensure that there is no cross contamination between the patients.

10

Although others have proposed calibration fixtures that compensate for the above-described variations in instrument performance, none have provided a simultaneous solution to both the calibration issue and the problems associated with the spread of infection in a medical setting. Furthermore, calibration devices that are designed to be re-used can become damaged by sunlight, temperature, humidity and other effects, which could lead to errors in calibration.

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One application of spectroscopic measurement systems involves detection of a bilirubin concentration in a human. Bilirubin is produced from the breakdown of hemoglobin in red blood cells. Under normal conditions, the bilirubin is conjugated by glucoronyl transferase, an enzyme present in the liver, and is then excreted through the biliary system.

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Newborn infants and prematurely born infants are particularly susceptible to hyperbilirubinemia. Hyperbilirubinemia describes the state where there is excessive

bilirubin in the body. Often this is due to the lack of functioning glucoronyl transferase enzyme in their liver, or excessive red blood cell breakdown associated with erythroblastosis fetalis.

One method for bilirubin testing includes blood based lab assay testing. The
5 "heel stick" blood lab assay is currently the only accepted methodology for quantitative bilirubin testing results in the United States. Of course, this invasive approach requires that blood be drawn to perform the test.

Non-invasive measurements of the bilirubin concentration would eliminate the need to draw blood samples from patients for bilirubin analysis. It would also
10 provide easy patient interface. It is known that bilirubin can be measured non-invasively by taking reflectance measurements from a patient's skin, from the aqueous of the eye, or from the sclera (white) of the eye, based on the fluorescent signature. Reflectance measurements can also be made on the tympanic membrane of the ear. This is possible because bilirubin from the blood stains the skin as well
15 as other tissues of the body. Jaundice refers to the condition when the bilirubin is visible in the skin and sclera.

Many attempts have been made to measure cutaneous bilirubin non-invasively. These attempts include the development of visual reference standards, and
20 transcutaneous reflectance spectroscopy to measure the absorption spectra of bilirubin, oxidized blood, and melanin, the dominant absorbers in the skin. The concentration of these pigments have distinct absorption spectra.

Reflectance bilirubinometers have obtained reasonable correlations between bilirubin levels determined transcutaneously and serum bilirubin concentrations in homogeneous patient populations. Unfortunately, these devices have failed to give satisfactory correlations when used over a heterogeneous population. Since patient populations are rarely homogeneous, transcutaneous bilirubin measuring methods have not been widely accepted clinically.

SUMMARY OF THE INVENTION

An object of the invention is to provide a measurement system with a disposable calibration device that is inexpensive and that helps to prevent contamination or infection.

Another object of the invention is to provide a spectroscopic system which uses a calibration device which provides an optically clear, scratch-free window between the optical instrument and the tissue or material to be measured.

It is also an object of the invention to provide a disposable calibration target configured for single use only.

Another object of the invention is to provide a simple and accurate apparatus and method of measuring a patient's bilirubin concentration.

A further object of the invention is to provide a system and method for comparing the optical characteristics of a first target material to optical characteristics of a second target material.

A measuring instrument embodying the invention transmits radiation to a material or tissue and receives and analyzes radiation transmitted through, reflected from or scattered from, or generated by the material or tissue being measured. In some embodiments, the radiation emitted by the instrument may be polarized, and 5 the polarization orientation of the transmitted, reflected/scattered or generated radiation may be analyzed by the instrument. Also, particular embodiments of the invention may combine multiple ones of the above listed techniques to arrive at a diagnosis of a patient, or to provide an analysis of a target material.

A measuring instrument embodying the invention may include a spectrometer 10 capable of determining the amplitude of radiation at any of a plurality of wavelengths. Alternatively, the measuring instrument may comprise a detector and one or more filters for selectively focusing radiation of specified wavelengths upon the detector. The measuring instrument could also comprise a plurality of filters and a corresponding plurality of detectors, where radiation from a target material passes 15 through the filters and onto the detectors so that each detector receives radiation at a different wavelength. The measuring instrument might also comprise a diffraction grating and a plurality of detectors, wherein the diffraction grating focuses radiation of predetermined wavelengths on respective ones of the plurality of detectors. Still further, the radiation analyzer may comprise a radiation detector and a linear variable 20 filter.

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In still other embodiments of the invention, a measuring system could include a plurality of emitter and detector pairs arranged in an array on the measuring instrument. Light output from the emitters could reflect/scatter/transmit from a target material or tissue or light could be emitted from the material or tissue, and the light would be received by the corresponding detectors. In another embodiment, the measuring system could include a single light source for illuminating a target material or tissue, and an array of detectors, such as a charge coupled device (CCD), for receiving light that is reflected/scattered/transmitted/emitted from the target material or tissue. Each of these embodiments would allow the measuring instrument to develop an image of the target material or tissue, or an image of reflective/transmissive/fluorescent properties of the target material or tissue.

A measurement instrument embodying the invention also may include one or more transmit and receive fiber optic waveguides for directing electromagnetic radiation to a material or tissue to be measured and for conducting radiation from a target material or tissue back to a sensor of the instrument. The instrument may be configured such that radiation transmitted from the instrument toward the material or tissue being measured is directed toward the material or tissue at an angle relative to a plane normal to the surface of the material or tissue so as to reduce backscattering effects.

A method and device embodying the invention may measure a bilirubin concentration in a patient using the amplitude of radiation reflected from a patient's

skin at first and second wavelengths representing a blood content of the skin, and at a third wavelength representing an uncorrected bilirubin concentration. Such a method and instrument may also utilize the amplitude of reflected radiation at fourth and fifth wavelengths that represent a melanin content of the patient's skin.

5 A measuring instrument embodying the invention may include a calibration device that includes a structure through which radiation can be transmitted. The calibration device may also include a removable calibration target arranged on said structure and capable of returning a portion of radiation output by the instrument back to a sensor of the instrument for purposes of conducting a calibration operation.

10 In alternate embodiments, radiation may be transmitted through the calibration target before passing to a sensor of the instrument. In still other embodiments, the calibration target may include a fluorescent or luminescent portion that emits fluorescent or luminescent radiation towards a sensor of the measuring instrument for purposes of conducting a calibration operation. The removable calibration target is configured to be removed from the structure of the calibration device after a calibration operation is completed, while the structure remains attached to the measuring instrument, so that radiation can pass through the structure during a subsequent measuring operation.

15 When the instrument is for medical diagnostic purposes, a calibration device embodying the invention may include a shield to prevent patient contamination or infection. In some embodiments, the calibration device may comprise both an

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infection shield and a calibration or reference target with known optical properties integrated into a single unitary element.

In preferred embodiments, the removable calibration target is configured such that a portion of the calibration target having predetermined optical characteristics is destructively altered when it is removed from a structure of the calibration device.

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As will be explained more fully below, configuring the calibration device so that it can only be used once can help to prevent patient infection or cross-contamination.

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A calibration device embodying the invention may also include an index matching substance, such as a gel, that can be interposed between a material or tissue being measured and a distal end of a measurement instrument.

15

In one method embodying the invention, a reference target is attached to an output end of a measuring instrument. A first measurement is then taken with a light source of the measurement instrument turned off. This is called a dark reference reading. Next, a measurement is taken on the reference target with the light source turned on. This is termed a reference reading. The reference target is then removed from the measurement instrument, and a first measurement is conducted on a patient or an object with the light source of the instrument turned off. This is termed a dark object reading. Next, a patient or object measurement is conducted with the light source turned on. This is termed an object reading. A ratio is then created with a difference between the object reading and the dark object reading in the numerator, and a difference between the reference reading and the dark

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reference reading being in the denominator. By creating a ratio of the differences, any variation in the light output of the measurement instrument or of the detector sensitivity cancels out to provide an accurate measurement result.

In addition, the reference reading, dark reference reading, skin reading and
5 dark skin reading can all be corrected for "stray light." The correction for stray light also helps to ensure that the measurement reading is more accurate. A method and formula for calculating and correcting for stray light is provided in the detailed description below.

Additional advantages, objects, and features of the invention will be set forth
10 in part in the description which follows, and in part will become apparent to those having ordinary skill in the art upon examination of the following, or may be learned from practice of the invention. The objects and advantages of the invention may be realized and attained as particularly pointed out in the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

15 Figure 1A shows a schematic view of a measurement system in a calibration mode;

Figure 1B shows a measurement system in a measurement mode wherein a calibration target has been removed and radiation is reaching a tissue or material to be measured;

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Figure 2A shows a schematic representation of a calibration device embodying the invention;

Figure 2B shows the calibration device of Figure 2A after a calibration target is removed from a window of the device;

5 Figure 2C shows a schematic sectional representation of another calibration device embodying the invention;

Figure 2D is a schematic representation of the calibration device of Figure 2C after a removable seal has been removed;

10 Figure 2E shows a schematic representation of the calibration device of Figure 2C mounted on a measurement instrument after a calibration target has been removed from the device;

Figure 2F is a schematic sectional representation of a calibration device embodying the invention;

15 Figure 2G shows the calibration device of Figure 2F mounted on a measurement instrument after a removable calibration target has been removed from the device;

Figure 3A is a schematic representation of another calibration device embodying the invention;

20 Figure 3B is a schematic representation of the calibration device of Figure 3A, positioned adjacent a material or tissue to be measured, with a calibration target partially removed from the device;

Figure 3C shows a measurement system embodying the invention which utilizes a disposable calibration device as shown in Figures 3A and 3B;

Figure 3D shows the measurement system of Figure 3C with the calibration device removed;

5 Figure 3E is a cross-sectional view of a measurement system embodying the invention that includes a spring loaded annulus at a distal end of the measurement instrument;

10 Figure 3F is a flow chart summarizing the steps involved in calibrating a measurement instrument and taking a measurement on a material or tissue using a method embodying the invention;

Figure 4 is a perspective view of a structure of a calibration device embodying the invention;

Figure 5A is a side view of a calibration device embodying the invention;

15 Figure 5B is a sectional view of another calibration device embodying the invention;

Figure 6 is a schematic representation of another calibration device embodying the invention.

Figure 7A is a schematic side view of another calibration device embodying the invention;

20 Figure 7B is a front view of the calibration device of Figure 7A;

Figure 8 is an exploded perspective view of a calibration target embodying the invention that could be used in a measuring system embodying the invention;

5 Figure 9 is an exploded perspective view of a combined calibration/reference target and infection shield embodying the invention that could be used in a measuring system embodying the invention;

Figure 10 is a plan view of another calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

Figure 11 is another plan view of a calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

10 Figure 12 is a plan view of another calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

Figure 13 is a sectional side view of a calibration device embodying the invention;

15 Figure 14 is an exploded perspective view of a calibration/reference target and infection shield that could be used in a measuring system embodying the invention;

Figure 15A is a side sectional view of a calibration device embodying the invention;

Figure 15B is a perspective view of the calibration device of Figure 15A;

20 Figure 16 is a plan view of another calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

Figure 17 is a side view of another calibration/reference device embodying the invention that could be used in a measuring system embodying the invention;

Figure 18 is a perspective view of another calibration/reference device embodying the invention that could be used in a measuring system embodying the invention;
5 invention;

Figure 19 is a plan view of another calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

Figure 20 is a plan view of another calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

10 Figure 21 is yet another embodiment of a calibration/reference target embodying the invention that could be used in a measuring system embodying the invention;

Figure 22 is a diagram of an external light source that can be used with a measuring instrument and transmissive calibration/reference device embodying the invention;
15 invention;

Figure 23 is a diagram showing a measuring instrument embodying the invention performing a calibration operation or a measurement operation utilizing an external light source;

Figure 24A is a diagram of a measuring instrument embodying the invention;

Figure 24B is a diagram showing a measuring instrument embodying the invention conducting a calibration/reference operation with a transmissive calibration target;

Figures 25A, 25B, and 25C show front, side and back views, respectively, of
5 a measurement instrument embodying the invention;

Figure 25D shows a measurement instrument embodying the invention in a
charging stand;

Figure 26A is a schematic diagram of certain elements of a measuring
instrument embodying the invention;

10 Figure 26B shows a cut away perspective view of an optical unit of the
measurement instrument of Figure 26A;

Figure 27 is a diagram showing a fiber optic bundle of a measurement
instrument embodying the invention adjacent a tissue or material being measured;

15 Figure 28 is a sectional view of the fiber optic bundle of Figure 27 as seen from
section line 28-28;

Figure 29 is a sectional view of the fiber optic bundle of Figure 27 as seen from
section line 29-29;

20 Figure 30 is a diagram showing transmit and receiving optical fibers of a
measurement instrument embodying the invention and the path of radiation emitted
or received by the optical fibers;

Figure 31 is a block diagram of parts of a measurement instrument embodying the invention;

Figure 32 is a flow chart showing the steps of a method embodying the invention for calculating a bilirubin concentration of a patient;

5 Figure 33 is a diagram showing the results of data taken using the method of Figure 24 versus a standard serum bilirubin (heel stick) method;

Figure 34 is a flow chart of another method embodying the invention for calculating a bilirubin concentration of a patient;

10 Figure 35 is a diagram showing the amplitude of light reflected from a patient's skin under two conditions, the first condition corresponding to blood in the patient's skin being 100% oxygenated and the second condition corresponding to the blood in the patient's skin having no oxygen;

15 Figure 36 is a diagram showing the amplitude of radiation reflected or scattered from a patient's skin for explaining how a corrected bilirubin concentration is calculated using a method embodying the invention;

Figure 37 is a flowchart of a method of performing bilirubin measurements on a patient embodying the invention;

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The terms "calibration target" and "reference target" are used interchangeably
20 in the following text to refer to a target having known optical properties. The

invention is applicable to both calibration targets and reference targets, and use of either term should not be construed as limiting. Also measuring instruments embodying the invention make use of electromagnetic radiation. The terms electromagnetic radiation, radiation and light are intended to be equivalent terms, all of which refer to electromagnetic radiation.

5

Figure 1A is a schematic view of a spectroscopic measurement system 3 in a calibration mode. The system 3 includes an instrument 10 which outputs electromagnetic radiation 39 and receives and analyzes radiation reflected back towards the device by a material or tissue 30 being measured, or that is generated by the material or tissue 30 in response to the radiation output by the instrument 10. 10 Alternatively, the instrument 10 may output, receive and analyze acoustic waves. Reference number 39 will be used to represent electromagnetic radiation or acoustic waves, just as reference number 10 will be used to represent an instrument that outputs either electromagnetic radiation or acoustic waves.

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The electromagnetic radiation 39 output by the instrument 10, or that is generated by a material or tissue or a calibration target, may lie within the visible, infrared, ultra-violet regimes, and/or within the rf, microwave and millimeter wave regimes. With regard to electromagnetic radiation 39, the instrument 10 can be a spectrometer, laser radar, radar or any other radiation measuring instrument that outputs radiation to a material or tissue 40, then measures some portion of a return signal.

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With regard to acoustic waves, the instrument 10 can be an acoustic measuring/imaging device that outputs acoustic waves and measures the return acoustic wave signal. The discussion that follows is drawn to a device that uses electromagnetic radiation, it being understood that an analogous discussion applies
5 for an instrument that uses acoustic waves.

During a calibration procedure, as shown in Figure 1A, radiation 39 is transmitted toward and through a shield 20 toward a calibration target 30. The shield 20 serves as a barrier between the instrument 10 and a material or tissue 40 to be measured, and hence functions to reduce contamination of the material or tissue 40.
10 One major (but not the only) purpose of the shield 20 is to guard against possible infection when living tissue 40 is measured. Hence, the shield 20 might also be referred to as an infection shield. A shield 20 must be at least partially transmissive to radiation 39 such that a portion of the emitted radiation passes through the window 20 to appear as radiation 39'.
15 Radiation 39' passes through a region 35 and reaches a surface 41 of the calibration target 30. The surface 41 can be the same material as the calibration target 30, or a specially applied layer. The surface 41 reflects or scatters radiation back towards the instrument 10, or emits florescent or luminescent radiation. Note that throughout this specification, reflection and scattering are used interchangeably and
20 are meant to indicate that radiation travels back toward instrument 10. Also, the region 35 can include a variety of adhesives, gels, pastes, or other materials.

Once the system 3 with the instrument 10 is calibrated, the calibration target 30 is removed, and the system 3 is ready to take measurements on a target material 40 through the shield 20. Figure 1B shows the system 3 in a measurement mode, wherein the calibration target 30 has been removed and radiation 39' is now reaching a tissue or material 40 to be measured through the shield 20.

Figure 2A shows a schematic representation of a calibration device 45 embodying the invention. The calibration device 45 includes a shield supporting structure 250 with a window 260. Together, the structure 250 and the window 260 comprise the shield 20 shown in Figure 1A. In alternative embodiments, the window 260 can be an opening in the structure 250, or a transmissive barrier. Any reference to a window should be read to encompass either an opening or a transmissive structure, where appropriate. Also, in this embodiment, the supporting structure 250 is shaped like a truncated cone. As a result, the window 260 is circular. It should be understood, however, that the shape of the shield structure 250 need not be limited to a cone-type shape, and the window 260 need not be limited to a circular shape.

The calibration device 45 also includes a calibration target 270 (corresponding to the calibration target 30 in Figure 1A) with a user graspable tab 280. The calibration target 270 is arranged in the window 260 of the structure 250.

The calibration device 45 receives radiation 39 from an instrument 10. The radiation 39 passes through the window 260 and the region 35 and reaches the surface 41 of the calibration target 270. The window 260 must be at least partially (and

preferably nearly completely) transparent to the radiation 39. The region 35 can include an adhesive, gel, or liquid which may act as an index matching agent, and/or free space. In one embodiment, the window 260 is statically charged with respect to surface 41 of calibration target 270. The static charge holds the calibration target 270 in place. Radiation 39 is then incident on the surface 41 of the calibration target 270.

If the calibration target 270 is to be reflective, it should be configured to have a known reflection spectrum for calibration purposes (note that the radiation 39 is scattered or reflected from the calibration target 270 back towards the instrument 10). For instruments 10 which perform measurements of intensity, independent of wavelength, a highly reflective surface 41 of the calibration target 270 may be advantageous. This might include radar, laser radar and interferometric type instruments. Note, however, that such instruments might also benefit from using a less reflective surface 41 on the calibration target 270.

Once a measurement system is calibrated, the calibration target 270 is removed from the window 260 by pulling on a user graspable tab 280, as shown in Figure 2B. The system 3 is now ready to take measurements on a material or tissue 40 through the window 260 of the calibration device.

Figures 2C through 2E show an embodiment of the calibration device that includes an index matching agent. As shown in these figures, the calibration device includes a structure 250, a calibration target 270 having a calibration surface 41 and an index matching agent 293 contained within the structure 250 and covered with a

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seal 290. The index matching agent 293 could be a liquid or a gel that aids the instrument in taking an accurate measurement.

To use a calibration device that includes an index matching agent, one would first remove the seal 290 using a user graspable tab 295. The calibration device, without the seal 290, is shown in Figure 2D. The calibration device would then be attached to a housing 298 of a measurement instrument, as shown in Figure 2E. The housing may include a window 294 designed to abut the index matching agent 293 when the structure of the calibration device is mounted on the instrument. A bundle of optical fibers 299, that transmit and receive radiation, may abut the other side of the window 294.

Once the structure 250 of the calibration device is mounted on the housing 298 of the measurement instrument, a calibration measurement would be performed while the calibration target 270 is still attached to the structure 250. After the measurement instrument has been calibrated, the calibration target 270 would be removed from the structure 250 so that measurements can be performed on a material or tissue. All or a portion of the structure 250 may be made of a flexible material so that the structure 250 can flex when the instrument is pressed against a target material, or the skin of a patient. This would cause the index matching agent 293 to completely fill the void between the target material/patient's skin and the window 294 of the measurement instrument.

Another calibration device embodying the invention is shown in Figures 2F and 2G. In this embodiment, the calibration device includes a structure 250 and a window 297. A calibration target 270 is attached to the structure 250 and an index matching agent 293 is trapped between the window 297 and the calibration target 270.

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The calibration target would be mounted on a housing 298 of a measuring instrument, as shown in Figure 2G. A bundle of optical fibers 299 can then abut a first side of the window 297 opposite the index matching agent 293. Once the calibration device is attached to the measurement instrument, a calibration measurement can be performed while the calibration target 270 is still attached to the structure 250. After calibration has occurred, the calibration target 270 could be removed so that measurements can be performed on a material or tissue.

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Figures 3A and 3B correspond to Figures 2A and 2B, but with radiation 39 entering from the right side, and the calibration target 270 attached to the window 260 within the structure 250. In this case, an outer annular ring 306 comes into contact with a tissue or material 40 to be measured. Structure 250 also includes an annular ring or ridge 312, which is intended to be used to secure the device 45 to an instrument 10 (not shown).

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Figure 3C shows a measurement system 3 which utilizes a disposable calibration device 45. Here, the measurement instrument 10 is an optical instrument, such as a spectrometer, and radiation 39 is electromagnetic radiation which can be in

the visible, UV and/or infrared regions. The system 3 includes a housing 343 which is easily graspable by a human hand. The instrument 10 is coupled to calibration device 45 via optical fibers 333. The calibration device 45 is inserted into an opening end 346 of a cone-shaped holder 358 of the housing 343. The cone shaped holder 358 can have any shape depending, among other things, on the shape of the calibration device. Hence, the holder 358 will alternatively be referred to as a calibration device receiving element. The holder 358 can be a separate piece, or part of the housing 343. It is preferable that the holder 358 be capable of receiving the calibration device 45 and allowing the calibration target to be readily removed from the calibration device so that a measurement may be performed on a material or tissue 40. The holder 358 should also allow the calibration device 45 to be easily removed so that the system 3 is again ready to receive a new calibration device 45.

A curved portion 366 of the housing 343 allows the user's hand to comfortably hold the system 3. A user can initiate a calibration or measurement, as the case may be, by pressing a push button 361 with his or her thumb. Once a calibration measurement has been performed, a user graspable tab 280 is used to remove the calibration target from the window 260 (not shown in this view), and the system 3 is ready to make a measurement on a material or tissue 40.

Figure 3D shows the same measurement system with the calibration device 45 removed. A new calibration device 45 must be inserted into the holding end 346 of the system 3, the above discussed process of calibration repeated, and the calibration

target 270 removed, before the measurement system 3 is ready to perform a new measurement. Alternatively, a cap 375 can be placed over the holding end 346 between measurements. In all of the above embodiments, the calibration target 270 can have calibration information fitted directly on the surface 41 of the calibration target 270. This calibration information can include a message read by the instrument 10, or a particular pattern that can be recognized by the instrument. In such a system, if a calibration target does not include the predetermined message or pattern, the instrument could be configured to shut down. This would prevent the use of unauthorized calibration targets, which would help to ensure the instrument 10 is always properly calibrated.

Figure 3E shows a cross-sectional view of a measurement instrument embodying the invention. The instrument includes a measurement device 10 coupled to an output end 370 of the system 3. An annulus 372, that surrounds a bundle of optical fibers 333, is mounted on the output end 370 of the system 3. The annulus 372 is mounted on the system 3 utilizing a spring 373, which biases the annulus 372 outward away from the measurement system 3. The annulus 372 may also be connected to a device that senses the position of the annulus 372 relative to the housing of the system 3.

According to one embodiment of the invention, the measurement device 20 functions independently of spring 373 in that a measurement can be made regardless of whether or not spring 373 is biased. According to another embodiment of the

invention, when a user performs a measurement using the measurement system 3, the user would push the instrument against a surface of a target material, or the skin of a patient, so that the annulus 372 moves inward, against the bias of the spring 373. The movement would be sensed by a proximity sensing device. The proximity sensing device could then be used to output a signal when the annulus 372 is pushed far enough into the measurement system 3 such that a measurement can be performed by the measurement system 3. In a measurement system including a spring biased annulus 373, the proximity sensing device could be used to disable the device when the annulus 373 is too far out, and to enable the device to take a measurement when the annulus 372 is pushed a sufficient distance into the device such that a measurement can be accurately performed. The proximity sensing device could be a simple switch having electrical contacts, or a light emitter and corresponding sensor. Alternatively, the proximity sensor could directly sense the proximity of an output end of the measurement instrument to a target material or tissue using an optical system or some other equivalent sensor, as would be well known in the art.

Figure 3F summarizes the steps involved for the system 3 to take a measurement on a material or tissue 40. In particular, step 382 involves placing a calibration device 45 on the end 346 of the system 3. At this point, the calibration device still has a calibration target 270 covering the window 260. A calibration measurement is performed by the system 3 at step 384 by pressing a push button 361,

which activates the measurement instrument 10. Step 388 involves removing the calibration target 270 from the window 260. Step 392 then involves performing a measurement on a tissue or material 40 to be measured. This might involve a single measurement or multiple measurements (if cross contamination is not an issue) on the same or a similar tissue or material. That is, multiple measurements might be taken in one vicinity, or at different locations on a material or tissue. The results of the multiple measurements could be averaged or interpreted to arrive at a measurement result. Finally, once the measurement or measurements have been completed, the calibration device 45 is removed, discarded, and replaced with a new calibration device 45 at step 396. Alternatively, a used calibration device 45 can be removed, discarded, and a cap 375 can be placed over the end 346 until a new measurement is to be made.

A calibration/reference device embodying the invention, that could be used with a measuring system embodying the invention, may be comprised of several parts. The first part is simply a device for anchoring a contamination/infection shield and a calibration/reference target to a measuring instrument. If the instrument is like the one shown in Figure 3C or 3E, a shield holder 110, as shown in Figure 4, can be used to attach an infection/contamination shield and a calibration/reference target to the nose portion of the measuring instrument.

As seen in Figures 4, 5A and 5B, the shield holder 110 has a plurality of finger-like projections 114 arranged in a cylindrical shape. Some or all of the projections

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114 may include a lip 116 which is engageable with the nose portion of the instrument to attach the device to the instrument. The projections might also engage a spring loaded mechanism like the one shown in Figure 3E. If the shield holder 110 is made from a flexible material, such as a molded plastic, the shield holder 110 can be snapped onto the nose of the instrument so that the lips 116 engage the nose.

5 A multilayer combined contamination shield and calibration target 200 can then be affixed to a front annular surface 112 of the shield holder 110, as shown in Figure 5A. In a preferred embodiment of the invention, the combined contamination shield and calibration target 200 is attached to the shield holder 110 with a layer of adhesive. The combined contamination shield and calibration target 200 may include a user graspable tab 202 for removing the calibration target after a 10 calibration or reference operation has been performed.

15 Of course a calibration target 200 could also be mechanically attached to the shield holder 110 by any type of mechanical attachment mechanism such as staples, clips, pins, etc. Figure 17, which is described in more detail below, shows an embodiment where a calibration target 206 is attached to a shield holder 110 with a plurality of pins 220 arranged around the periphery of the shield holder 110.

20 In an alternate embodiment, as shown in Figure 5B, an infection shield 204 may be separately mounted to the shield holder 110. The infection shield 204 could simply be a clear plastic portion of the shield holder 110, which is integrally molded with the shield holder 110. The infection shield 204 could also be a substantially

transparent film that is attached to the shield holder 110. A calibration target 206 could then be attached to the front annular surface 112 of the shield holder 110 via an adhesive layer or some type of mechanical attachment device. The calibration target 206 would include a user graspable tab 202 for aiding removal of the calibration target after a calibration or reference operation has been performed.

Figure 6 shows a calibration device 45 according to another embodiment of the invention. Here, a landing annulus 690 is affixed to the structure 250. The landing annulus 690 serves to fix the angle at which radiation is incident on the surface 680 of a material or tissue 40 being measured. The landing annulus 690 is preferably transparent to radiation 39. Calibration occurs, as before, using the calibration target 270. The calibration target 270 is then removed, and the annulus 690 remains in place. The measuring instrument, is then placed on the surface 680, such that the annulus 690 lies flat on the surface 680. This ensures that radiation 39 is incident approximately normal to the surface 680, as it was to the surface 41 of the calibration target 270. On the other hand, depending on the type of measurement, it may be preferable, due to unwanted spectral reflections, to have radiation 39 incident at an angle relative to an axis normal to the surface 680. The landing annulus 690 can be a separate piece affixed to the structure 250 and comprised of any type of rigid material such as various plastics. If infection to the surface 680 of tissue 40 is an issue, then the landing annulus 690 should be removable from the structure 250. Alternatively, annulus 690 can simply be an extension of window 260 itself.

The structure 250 is preferably fabricated from molded plastic with a smooth window zone defined for the window 260. Using plastic molding allows the structure 250 to be fabricated at low cost and in a wide variety of shapes and sizes. The calibration target 270 can also be fabricated from plastic and may also have a dye or other material added to the surface 41 to provide sufficient spectral detail to effect the necessary calibration. The calibration target 270 can be attached to the window section 260 in such a way that once removed, it cannot be readily re-attached. One implementation is to fabricate the calibration target 270 using a statically clinging type plastic, and to fabricate structure 250 using an appropriate material such as an acrylic called polymethyl methacrylate (PMMA), both of which are available from 3M Corporation.

Figure 7A shows a side view of a calibration device 45 according to yet another embodiment of the invention. Here, the calibration target 270 is held in place by a ridge 700 alone, or together with static cling between the calibration target 270 and the window 260. The ridge 700 can be part of the window 260, or a separate piece. Figure 7B shows the calibration device 45 as viewed from above.

A calibration/reference target that could be used with a calibration target embodying the invention is shown in Figure 8. The target includes a calibration layer 470 having a central portion 474 with known optical properties. A user graspable tab 472 is formed as a part of the calibration layer 470. Also, a double-sided adhesive layer 440 is used to attach the calibration layer 470 to a shield holder 110,

as shown in Figure 5B. In alternate embodiments, the adhesive layer 440 can be used to attach the calibration layer 470 to an infection/contamination shield layer which is then attached to the shield holder 110, as shown in Figure 5A. Also, the adhesive layer 440 could be used to attach the calibration layer 470 directly to a measuring instrument. In still other embodiments, the double-sided adhesive layer 440 could be replaced with an adhesive that is applied to the calibration layer 470 in a liquid, gel or paste form.

In preferred embodiments, the calibration layer 470 and the double-sided adhesive layer 440 are carefully constructed so that when the calibration target is removed from a shield holder, the target portion 474 in the center of the calibration layer 470 will tear in a predetermined manner. To that end, the calibration layer 470 may include a reduced strength portion 480, which could be a slit, a perforation or a crease. The reduced strength portion 480 in the embodiment shown in Figure 8 is a perforation that extends from a peripheral edge of the calibration layer 470, towards the central area 474. When a user grasps the tab 472 and pulls on the tab to remove the calibration layer 470 from a shield holder, the calibration layer 470 will tend to tear along the reduced strength portion 480.

In the embodiment shown in Figure 8, the adhesive layer 440 has a horseshoe shape such that a portion of the calibration layer 470 having the reduced strength portion 480 is aligned with the gap in the adhesive layer 440. Also, in a preferred embodiment, a first side 442 of the adhesive layer 440 will have a relatively low

adhesive strength, and the opposite side of the adhesive layer 440 will have a greater adhesive strength. In this configuration, the lower adhesive strength side 442 of the adhesive layer 440 is used to attach the calibration layer 470 to a shield holder. When a user pulls on the tab 472 to remove the calibration layer 470, the lower adhesive strength side 442 will separate from the shield holder before the higher adhesive strength side separates from the calibration layer 470. Thus, the adhesive layer 440 is fully removed along with the calibration layer 470. Also, because of the gap in the adhesive layer 440, the portion of the calibration layer immediately to the right of the reduced strength portion 480 will tend to remain attached to the shield holder while the portion of the calibration layer 470 adjacent the tab and located beneath the gap in the adhesive layer 440 will pull upward and away from the shield holder. This will cause the calibration layer 470 to begin to tear along the reduced strength portion 480. As the user continues to pull on the tab 472, the tearing of the calibration layer 470 will tend to continue across the center portion 474 having the optical properties used to perform a calibration operation.

If a liquid, gel or paste adhesive is used to attach the calibration layer 470 to a shield holder 110, there will not be varying adhesive strengths. However, in such an embodiment it would be advantageous if the adhesive had a greater affinity for the calibration layer 470 than for the shield holder 110. In this case, most, if not all, of the adhesive would remain attached to the calibration layer 470 as it is removed from the shield holder 110. Thus, no adhesive remaining on the shield holder 110 would

contact the skin of a patient or a surface to be measured when the instrument and attached shield holder 110 are used to take a measurement.

- Similarly, if some type of mechanical attachment mechanism is used to attach the calibration layer 470 to a shield holder 110, it may be advantageous if the 5 mechanical attachment mechanism is more firmly attached to the calibration layer 470 than to the shield holder 110. This would result in the attachment mechanism being removed from the shield holder along with the calibration layer, leaving the shield holder 110 free of any protrusions when used to take a measurement. For instance, in the embodiment shown in Figure 17, the pins 220 attaching the 10 calibration target 206 to the shield holder 110 could be more firmly attached to the calibration target than the shield holder 110. The cylindrical shafts of the pins 220 would extend through the annular portion 112 of the shield holder 110. Ends of the pins 220 that protrude out the back side of the annular portion 112 could have a slightly enlarged diameter, thus holding the pins 220 and the attached calibration 15 target 206 firmly to the shield holder 110. When the user pulls the calibration target 206 away from the shield holder 110, the pins 220 will pull out of the holes in the annular portion 112. Also, by arranging the pins in a particular orientation with respect to the user graspable tab 202 of the calibration target 206, the calibration target can be caused to tear or separate in a predetermined manner.
- 20 Once a calibration layer 470 has been completely removed from a shield holder, the central portion 474 of the calibration layer 470 should be irrevocably

damaged so that the calibration layer 470 cannot be re-used for a new calibration operation. In the embodiment shown in Figure 5B, because the side of the adhesive layer 440 in contact with the calibration layer 470 has a greater adhesive strength than the side 442 which was attached to the shield holder, all of the adhesive layer should remain attached to the calibration target and be removed from the shield holder along with the calibration layer 470.

As mentioned above, the calibration target shown in Figure 8 is intended to be used with a shield holder 110 as shown in Figure 5B. This type of shield holder 110 includes its own integral infection/contamination shield 204.

In an alternate embodiment, as shown in Figure 9, both a calibration target and an infection/contamination shield are attached to the exterior of a shield holder. In this embodiment, a first double-sided adhesive layer 410 is attached to a front edge 112 of a shield holder 110, like the one shown in Figure 5A. The opposite side of the adhesive layer 410 is then attached to a infection/contamination shield 420. In a preferred embodiment, the infection/contamination shield 420 is substantially transparent. An adhesive layer 440 and a calibration layer 470 are then attached to the infection shield 420. The adhesive layer 440 and the calibration layer 470 have generally the same properties as those described for the embodiment shown in Figure 8. That is, a first side 442 of the adhesive layer 440 has a relatively low adhesive strength, and the opposite side of the adhesive layer, which is attached to the calibration layer 470, has a greater adhesive strength. Thus, when a user pulls the tab

472 of the calibration layer 470 and removes the calibration layer, both the calibration layer and the adhesive layer 440 are removed. This leaves just the infection/contamination shield 420 attached to the shield holder 110 and the instrument 100. Of course the double-sided adhesive layers 410 and 440 could also
5 be replaced with a liquid, gel or paste adhesive, or with a mechanical attachment device, as described above.

Once a calibration/reference operation has been conducted, and the calibration target is removed, the instrument can be used to conduct a measurement on a patient or an object. In one embodiment, light generated by the instrument
10 passes through the infection shield 420, strikes the patient or object, and is reflected back through the infection shield 420 to a detector of the device. In an alternate embodiment, light generated by the instrument would pass through the infection shield 420, strike the patient or object, and the target patient or object would emit
15 fluorescent or phosphorescent emissions in response to the emitted light. The fluorescent or phosphorescent emissions would pass back through the infection shield and would be detected by the instrument. After a patient or object measurement has been completed, the shield holder 110 and the attached infection shield 420 are removed from the instrument 100 and disposed of.

The calibration layer 470 can have a reduced strength portion 480 configured
20 in many different ways. In the embodiments shown in Figures 8 and 9, the reduced strength portion extends from a peripheral edge towards a center 474 of the

calibration layer 470. This encourages the calibration layer to tear across the center portion 474, which is the portion having optical properties used to calibrate a measuring instrument. In preferred embodiments, the reduced strength portion 480 does not extend beyond the annular radial width of the adhesive layer 480 so that light cannot penetrate through the calibration layer 470 and affect a calibration or reference operation.

In the embodiment shown in Figure 10, a calibration target 270 can be manufactured with two user graspable tabs at its sides. Here, two pull tabs 531 and 533 are attached to two halves 535 and 537 of the calibration target 270. Between the two halves 535 and 537 is a mechanical perforation 539. When the calibration target 270 is pulled away from a structure of the calibration device by one of the tabs, it breaks along perforation 539, thereby making it difficult or impossible to reuse. The remaining half of the calibration target 270 can then be pulled away using the remaining tab.

In other alternate embodiments, as shown in Figures 11 and 12, the reduced strength portion can have different configurations. In the embodiment shown in Figure 11, the reduced strength portion 480 traverses a path across the central region 474 of the calibration layer 470. In the embodiment shown in Figure 12, the reduced strength portion 480 proceeds in a direct line across the center 474 of the calibration layer 470. Each of these embodiments is intended to ensure that as the calibration

layer 470 is removed, the central portion 474 used to calibrate the instrument is altered in a destructive manner so that the calibration layer cannot be reused.

In still other embodiments, a cutting device could be incorporated into the calibration layer 470, or into the shield holder 110 or the instrument itself. One such embodiment is shown in Figure 16, where a wire or monofilament 478 is attached to or embedded in the calibration layer 470. The wire or monofilament 478 will cause the calibration layer 470 to tear in a predetermined manner when a user pulls on the tab 472. Although Figure 11 shows the wire or monofilament extending only partway across the calibration layer 470, the wire or monofilament could extend further or completely across the calibration layer 470. The wire or monofilament could also be arranged in a pattern, like the reduced strength portion 474 shown in Figure 11.

In alternate embodiments, a wire or monofilament could also be attached to the shield holder. In the embodiment shown in Figure 18, a wire or monofilament 230 is stretched across the back of the calibration layer 200, with ends of the wire or monofilament being attached to the shield holder 110. Also, the wire or monofilament 230 could be replaced with any other type of cutting device that will cause the calibration layer 470 to tear or separate in a predetermined manner when being removed from a measuring instrument.

If the measuring instrument 100 embodying the invention is configured so that only a single patient or object measurement may be conducted after each calibration

operation, use of the calibration device can help to prevent patient infection or patient or object cross-contamination.

When a user attempts to use the measuring instrument, a shield holder with an infection/contamination shield and a calibration target will first be attached to the instrument. Next, a calibration/reference operation will be performed. Once the calibration/reference operation is complete, the user will grasp a tab on the calibration target and pull on the tab to remove the calibration target. This will cause the calibration target and any attached adhesive layer to be removed from the shield holder. The act of removing the calibration target will destroy at least the portion of the calibration target having the optical properties used to calibrate/reference the instrument. Thus, it will be impossible to reuse the calibration target. The user would then proceed to conduct a patient or object measurement with the shield holder and infection shield still attached to the instrument. The results of the measurement can then be noted or recorded.

Because the instrument will not perform a second patient or object measurement without first performing another calibration/reference operation, the user will be forced to remove both the shield holder and the infection shield and replace it with a new device that includes a new calibration target. The user will be forced to perform another calibration operation before the device can be used to perform another patient or object measurement. For this reason, it should be impossible for the device to be used to take two measurements on two different

patients or objects using the same shield holder and infection/contamination shield. This prevents cross-contamination between different patients or objects.

Also, an interlock mechanism in the measuring instrument may interact with a shield holder to inform the instrument when a shield holder is removed. The 5 instrument can then be configured so that no patient or object measurements can be performed once a shield holder has been removed from the instrument. This should discourage users from attempting to conduct a measurement without an infection/contamination shield in place, thereby reducing the opportunity for patient or object cross-contamination. Similarly, the interlock mechanism could be 10 configured to prevent more than one patient or object measurement cycle from being performed before a shield holder is removed and another one is inserted.

In a preferred embodiment of the invention, the shield holder is configured as shown in Figure 5A, and a combined infection/contamination shield and calibration target 200 will be constructed as shown in Figure 14. In this embodiment, a first 15 double-sided adhesive layer 410 is used to attach the combined infection/contamination shield and calibration target to the shield holder 110. The opposite side of the double-sided adhesive layer 410 is adhered to a shield layer 420. Next, a clear release liner 430 is attached to the infection shield 420. The release liner 430 will remain permanently attached to the infection shield 420, 20 but will provide a controlled release of the remaining portions of the combined infection shield and calibration target.

Next, a second double-sided adhesive layer 440 is attached to the release liner 430. As in the previous embodiments, a gap is formed in the adhesive layer 440. Next, a spacer layer 450 is attached to the opposite side of the second adhesive layer 440. The spacer layer 450 serves to space a calibration layer a precise distance from an emitting end of an instrument to which the device is attached. A third double-sided adhesive layer 460 then attaches a calibration layer 470 to the spacer layer 450.

The double sided adhesive layers 410, 440 and 460 could all be replaced with a liquid, gel or paste adhesive, or by a mechanical attachment device, as explained above.

The central portion 474 of the calibration layer 470 will be exposed to light emitted by an emission end of an instrument to which the device is attached. Also, reduced strength portions are formed in the spacer layer 450, the third double-sided adhesive layer 460 and the calibration layer 470. As explained above, the reduced strength portions cause the calibration layer 470 to tear in a predetermined manner when the calibration layer 470 is removed from the remaining portions of the device. Also, the reduced strength portions are oriented in a predetermined manner with respect to the gap in the second double-sided adhesive layer 440. Preferably, the reduced strength portions are positioned adjacent one side of the gap. When the device is oriented in this manner, pulling on the tab 472 of the calibration layer 470 causes the calibration layer to tear along the reduced strength portion 480 and to irrevocably damage the central portion 474 of the calibration layer 470.

Of course, the reduced strength portions could also be replaced by a cutting device, as explained above, to cause the calibration layer to tear or separate in a predetermined manner.

In alternate embodiments, the shield holder could be configured as shown in Figure 13. In this embodiment, the narrower portion of the shield holder is to be attached to a measuring instrument, and the larger diameter flared portion 112 extends away from the device. A flexible annular ring of material 210 on the rear of the shield holder may engage projections on the nose portion of a measuring instrument. In this embodiment, a combined infection/contamination shield and calibration target 200 is located adjacent the back side 208 of the shield holder 110, instead of being located on the front end 112. The combined infection/contamination shield and calibration target 200 still includes a user graspable tab 202 which can be pulled to remove the calibration target. This embodiment, like the embodiment shown in Figure 5B, could have an infection shield mounted on the shield holder and a separate calibration target which is adhered to the shield holder or the infection/contamination shield.

Another alternate embodiment of a calibration/reference device is shown in Figures 15A and 15B. In this embodiment, a calibration target holder 125 has a cup-like shape. A calibration target 126 may be mounted on the inside of the holder 125, as shown in Figure 15A. Alternatively, if the holder 125 is transparent, the calibration target 126 could be mounted on the outside of the holder 125. The holder

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125 could be formed of any rigid or semi-rigid material. In a preferred embodiment, the holder 125 would be made of molded plastic. The calibration target 126 could be pre-mounted on the holder 125, such that the entire assembly can be used for a period of time, then discarded. Alternatively, the calibration target 126 could be 5 removably mounted on the holder 125, such that the holder 125 can be re-used multiple times with different calibration targets 126. In this instance, the calibration target 126 could include a user graspable tab 127 that aids removal of the calibration target 126 from the holder 125.

To use this type of calibration device, the user would place the calibration 10 device over the detector of a measuring instrument. For instance, the calibration device could be placed over the nose of a measuring instrument. The measuring instrument would then conduct a calibration operation using a portion of the calibration target 126 having known optical properties. The user would then remove the calibration device from the measuring instrument and conduct a measurement on 15 a target object or tissue.

An embodiment like the one shown in Figures 15A and 15B could be used with a measuring device that does not require a calibration operation to be performed prior to each measurement. This embodiment could be used for periodic calibration of a measuring device. The holder would ensure that the calibration target is correctly positioned relative to the light source and detector of the measuring 20 instrument. Also, the sidewalls of the holder 125 would serve to block outside light

from reaching a detector of the device, thereby ensuring the calibration operation is accurate.

In a preferred embodiment of the device, the calibration target 126 would be removably mounted on the holder 125. The user would obtain a calibration target 126 and first place the calibration target 126 on the inside of the holder 125. The user would then conduct a calibration operation as described above. After the calibration operation has been performed, the user could remove the calibration target 126 from the holder 125 using the user graspable tab 127, so that the holder can be re-used with another calibration target 126.

Either of the calibration targets shown in Figures 8 and 9 could be used with the holder 125 shown in Figures 15A and 15B. If the calibration target shown in Figure 8 is used, the double sided adhesive layer 440 could be used to attach the calibration layer 470 to the inside of the holder 125. In this instance, the calibration layer 470 would have known optical properties on the side of the calibration layer 470 opposite the adhesive layer 440, which is the side that would face the detector of a measuring instrument.

If the calibration target shown in Figure 9 is used, an additional adhesive layer on the side of the calibration layer 470 opposite the adhesive layer 440 could be used to attach the calibration device to the holder 125. In this instance, when the holder is placed over the output end of the measuring instrument, the double sided adhesive layer 410 would be pressed against and adhere to the measuring instrument. Then,

after a calibration operation has been performed, when the holder 125 is removed from the measuring instrument, it will leave the entire calibration target attached to the measuring instrument. The user would then remove the calibration layer 470, and its attached adhesive layer 440, so that the shield layer 420 and the double sided adhesive layer 410 remain attached to the measuring instrument. The instrument could then be used to conduct measurements, and the shield layer 420 would act as a contamination or infection shield. Also, in alternative embodiments, the adhesive strength of the adhesive layers could be designed such that removal of the cover 125 from the measuring instrument, after a calibration operation, will cause the calibration layer 470 and adhesive layer 440 to also be removed from the measuring instrument. This would leave the measuring instrument, with the shield layer 420 and adhesive layer 410, ready to perform a measurement operation. The user could then remove the calibration layer 470 from the holder 125 so that the holder 125 can be re-used. Alternatively, the holder 125 and the attached calibration layer 470 and adhesive layer 440 could simply be discarded.

Also, the portion of a calibration/reference target having known optical properties need not be simply reflective. In an alternate embodiment, a target layer of a calibration device embodying the invention could include a fluorescent portion which emits fluorescent electromagnetic radiation in response to an excitation light. An embodiment of a fluorescent calibration layer is shown in Figure 19. In this embodiment, a fluorescent portion 473 is centered on the calibration layer 470.

When a calibration device that includes a fluorescent calibration layer is attached to a measuring instrument, light from a light source of the measuring instrument can be used to excite the fluorescent portion 473. The fluorescent portion 473 would then emit fluorescent electromagnetic radiation, which can be detected by a detector of the measuring instrument. The fluorescent light emitted by the fluorescent portion 473 may be at a different wavelength than the light used to excite the emissions. Thus, a fluorescent calibration device can be used to calibrate an instrument for light emissions in a different portion of the spectrum than would be possible with a reflective calibration device.

Also, a calibration/reference operation performed with a fluorescent calibration/reference target could be designed to determine time characteristics of the fluorescent target. For instance, the fluorescent target could be illuminated with a relatively short duration burst of excitation light, then the fluorescent emissions from the fluorescent target could be monitored to determine the amount of time that elapses before an amplitude of the fluorescent emissions decay below a threshold value. The details of such a method are provided in U.S. Patent No. 5,348,018 to Alfano et al, the contents of which are hereby incorporated by reference.

In an alternate method of conducting a calibration/reference operation with a fluorescent target, the fluorescent target could be illuminated with an amplitude modulated beam of excitation light. Because an amplitude of the excitation light modulates with time, an amplitude of the fluorescent light would also modulate with

time. A detector of a measuring instrument could monitor the fluorescent light generated by the fluorescent target and compare the amplitude modulation of the fluorescent light with the amplitude modulation of the excitation light. A phase shift between the excitation light and fluorescent light provides an indication of the time characteristics of the fluorescent target. Also, a demodulation factor, which represents a ratio of the amplitudes of the excitation light to the amplitudes of the fluorescent light could be used, in conjunction with the phase shift, to determine properties of the fluorescent calibration device. Details of such a method are provided in U.S. Patent No. 5,628,310 to Rao et al., the contents of which are hereby incorporated by reference.

In still other methods of using a fluorescent calibration/reference target, polarization characteristics of fluorescent light generated by the target, with respect to a polarization of the excitation light, can be used to determine time characteristics of the fluorescent target. In this method, a polarized excitation light would illuminate the fluorescent target. The detector mechanism of the measuring instrument would be configured to determine polarization characteristics of fluorescent light output by the fluorescent target in response to the excitation light. The polarization characteristics of the fluorescent light, with respect to the polarization of the excitation light could also be used to determine time characteristics of the fluorescent target. Details of such a method are provided in

U.S. Patent No. 5,515,864 to Zuckerman, the contents of which are hereby incorporated by reference.

In yet another embodiment, as shown in Figure 20, a calibration layer 470 includes a central region having a fluorescent portion 473 and a portion 474 having known scattering/reflection properties. When a calibration device including a calibration layer as shown in Figure 20 is mounted on a measuring instrument, light emitted from a light source of the instrument can both scatter/reflect off the portion 474 having known properties, and the light can excite fluorescent emissions from the fluorescent portion 473. The scattered or reflected light, and fluorescent emissions from the fluorescent portion 473 can be detected by a detector of the measuring instrument and used to calibrate or reference the instrument.

In still another embodiment, as shown in Figure 21, a fluorescent portion 473 may be centered within a region 474 having known scattering/reflective properties. Alternatively, the portion having known scattering/reflective properties could be centered in a larger fluorescent portion. When a target layer 470, as shown in Figure 21, is incorporated in a calibration device embodying the invention, both light scattered by the portion 474 and fluorescent light emitted by the fluorescent region 473 can be used in a calibration or reference operation.

The two portion calibration layers 470 shown in Figures 20 and 21 allow for a calibration operation to rely on light having different wavelengths. The light reflected from the portion 474 having known optical properties will be at the same

wavelength as the light emitted by the measuring instrument. Fluorescent light generated by the fluorescent portion 473 will be at a different wavelength. This type of calibration/reference operation could be particularly useful for measuring instruments that utilize light at more than one wavelength to conduct a measurement operation. This type of calibration/reference operation could also be useful for a device that utilizes both fluorescent light generated by a target object, and light that is scattered or reflected from the target object to conduct a measurement operation.

5 Also, even when a calibration target having a fluorescent portion is used, by selectively receiving only the same wavelengths that were emitted by the measuring instrument, one can conduct a calibration based on scattered light. By selectively receiving only the wavelengths corresponding to fluorescent light generated by a target, one can conduct a calibration operation based only on the fluorescent light, thereby preventing reflectance/scattering properties of the target from affecting the calibration operation.

10 Each of the methods of measuring fluorescent radiation described above could also be used by a measuring system embodying the invention to measure fluorescent light that is generated by a target object or a target tissue of a patient. For instance, after a calibration or reference operation has been conducted with a fluorescent calibration target, the calibration target would be removed, leaving a structure of the calibration device attached to the measuring instrument. The measuring instrument 15 could then be used to excite and measure fluorescent radiation from a target object

or tissue. In a preferred embodiment, excitation light from the measuring instrument would be used to excite fluorescent emissions from a target object or tissue. The fluorescent emissions would pass through the structure of the calibration device that remains on the instrument, to a detector of the instrument, which measures the 5 fluorescent emissions. Such a target object or tissue measurement could be conducted by using the burst and monitor method, the phase shift method, or the polarization sensing method.

In a method embodying the invention, the measuring instrument first takes 10 readings against a reference target, then takes readings against the skin of a patient or the surface of an object. The patient or object readings are then compared with the reference target readings to provide a meaningful output value. This output value may be expressed as an optical density (OD). A formula for calculating an optical density in a method embodying the invention is shown below in Equation (1).

$$\text{OD} = -\log_{10} (\text{Skin} - \text{SkinDark}), \quad (1)$$

15 $(\text{Ref} - \text{RefDark}),$

In a method embodying the invention, the measuring instrument is used with the reference target to obtain two values. First, a reading is taken against the reference target with a light source of the instrument turned off. This is referred to as a dark reference reading, which is abbreviated as RefDark in Equation (1). Next,

a reading is taken on the reference target with a light source of the measuring instrument turned on. This is referred to as a reference reading, which is abbreviated Ref in Equation (1). Both of these measurements would typically be conducted at a particular wavelength.

5 Next, two readings are taken on a patient's skin or on an object. The first reading is taken with the light source turned off to provide a dark skin reading. This is abbreviated SkinDark in Equation (1). Next, a reading is taken against the skin of the patient or on the object with the light source of the measuring instrument turned on to obtain a patient/object reading. This is abbreviated Skin in Equation (1). The dark skin reading is then subtracted from the skin reading to provide a corrected patient/object reading. The dark reference reading is also subtracted from the normal reference reading to provide a corrected reference reading. A negative logarithm is then taken of the ratio of the corrected patient reading to the corrected reference reading. This provides an optical density value which can be used to 10 diagnose a condition of the patient.

15 In alternate methods embodying the invention, a plurality of dark skin readings and normal skin readings may be conducted at multiple different locations on a patient's skin. The difference between the normal skin reading and the dark skin reading at each of the different locations can then be averaged to provide the 20 value for the numerator of Equation (1).

Furthermore, in alternative methods embodying the invention, two or more patient readings may be conducted at different wavelengths, and the results of each of the readings may provide a plurality of different optical density values that are then combined to determine a condition of the patient.

5 Still further, both the skin and reference readings described above may be corrected for "stray light." Theoretically, there is no light with a wavelength lower than 350 nm or with a wavelength higher than 850 nm. Signal levels detected at such wavelengths are considered "stray light." A method for correcting for stray light is described below with reference to Equation (2).

10

$$(I(\lambda))_s = (I(\lambda) - [I(330) - \frac{I(330) - I(900)}{(900-300)} * (\lambda-330)]) \quad (2)$$

15

If $I(\lambda)$ represents a corrected skin reading or a corrected reference reading, as described above, these readings can be corrected for stray light using Equation (2) shown above. The correction for stray light requires that the intensity of light be measured at 330 nm to provide a value $I(330)$, and that the intensity of light at 900 nm be measured to provide a value $I(900)$. These values are then inserted in Equation (2), shown above, to provide a stray light corrected intensity value $(I(\lambda))_s$. These stray light corrected intensity values for the corrected skin intensity and the corrected reference intensities are used in Equation (1) above to provide an optical density value which can be used to diagnose a condition of a patient.

Furthermore, a measuring system embodying the invention could be configured to measure light from a target object or tissue at more than one wavelength. For instance, in embodiments where light from the measuring instrument illuminates the target object or tissue and is scattered or reflected back to the measuring instrument, a detector of the instrument could measure the reflected or scattered light at multiple wavelengths.

In still other embodiments of the invention, the target layer 470 of a calibration target could be partially transmissive so that light transmitted through the target layer can be used to perform a calibration or reference operation. For instance, in the embodiment shown in Figure 8, the central region could have known transmissive properties so that light transmitted through the central region 474 may be used to perform a calibration or reference operation. Two methods for performing a calibration or reference operation using a transmissive calibration target will now be described with reference to Figures 22, 23, 24A ad 24B.

Figure 22 shows an external light source that can be used to perform a transmissive calibration or reference operation, and to conduct a transmissive measuring operation. The external light source 240 includes a light source 242, which can be in the form of an incandescent or fluorescent bulb, a light emitting diode, a laser, or any other device capable of generating electromagnetic radiation. An aperture 244 allows light from the light source 242 to escape the device. A slot 246,

or any other type of mechanical attachment mechanism, can be used to mount a sample to be measured in the aperture 244 of the light source 240.

Figure 23 shows a measuring instrument 100 being used to conduct a calibration or measurement operation using the external light source 240. If a calibration operation is to be performed, the light source 242 is turned on, and a calibration or reference device is mounted on the measuring instrument 100. The calibration device would include a calibration/reference target mounted on a shield holder 110. The calibration device is then pressed against the aperture 244 of the external light source 240. Light from the light source 242 passes through the aperture, and a portion of the light also passes through the calibration device. The light transmitted through the calibration device is received by a detector within the measuring instrument 100 and is used to conduct a calibration or reference operation.

In some embodiments of the device, a clear window 248 may be mounted in the aperture 244, and the calibration target may be pressed directly against the window 248.

Once a calibration or reference operation has been successfully performed, the calibration layer of the calibration device would be removed so that the device is ready to conduct a patient or object measurement. Removal of the calibration device could leave a shield holder 110 and an associated infection shield attached to the measuring instrument 100. An object to be measured may then be mounted on a slide 248 that is inserted into the aperture 244 of the external light source 240. The

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shield holder 110, without the calibration target, would then be pressed against the slide 248, and the measurement device would be activated to conduct a measurement. Light from the light source 242 would pass through the slide 248, the sample mounted thereon, and the infection shield and shield holder 110, and the transmitted light would be detected by a detector of the measuring instrument 100. The transmitted light would then be used to conduct a measurement operation.

This type of an embodiment could be useful for measuring optical properties or colors of objects capable of being mounted on slides 248 that are inserted into an external light source 240. In alternate embodiments, the measurement operation could be performed directly on an object without the use of the external light source 240. In this embodiment, the external light source 240 would be used only to perform a calibration or reference operation with a transmissive calibration target.

In the embodiment shown in Figures 24A and 24B, a light source of the measuring instrument would be used to conduct a transmissive calibration and/or measuring operation. The measuring instrument 100 would include a means for applying light to a calibration/reference target mounted on the instrument 100. The means could include a light source inside the instrument 100 which transmits light through an optical fiber to a light head 251. In alternate embodiments, the light head 251 could include an integral light source. In either event, the light head 251 may be attached to a retractable tether 252 for holding the light head 251 in place on top of the instrument 100 when it is not in use. If an optical fiber is used to conduct light

from a source inside the instrument to the light head 251, the optical fiber could be inside the tether 252.

With an embodiment like the one shown in Figures 24A and 24B, a shield holder 110 and an attached transmissive calibration target would be mounted on a nose portion 104 of the measuring instrument 100. Next, the retractable light head 251 would be pulled out of the device and placed over the transmissive calibration target attached to the shield holder 110. The device would then be activated so that light is emitted from the light head 251, is transmitted through the transmissive target, and is detected by a detector of the instrument 100 so that a calibration/reference operation may be performed.

Once a calibration/reference operation has been performed, the light head 251 could then be retracted back into the measuring instrument, and the calibration target would be removed from the shield holder 110. This would place the instrument in a condition ready for a patient or object measurement. The measurement operation could be conducted such that light emitted from the nose portion 104 of the instrument is reflected/scattered from the target object and is detected by the instrument. Alternatively, the light head 251 could be used to provide light for a measurement operation.

In some of the embodiments described above, a calibration operation has relied on light that is reflected/scattered from, transmitted through or emitted by, a portion of a calibration target having known optical properties. This could involve

determining an amplitude of the reflected/scattered/transmitted/emitted light at one or more wavelengths. In other devices and methods embodying the invention, the radiation output to the calibration target could have a particular polarization orientation. The measuring instrument could then be configured to determine a polarization orientation of the reflected/scattered/transmitted/emitted light. Such a method could rely on the relative attenuation of a polarized or depolarized component of reflected/scattered/transmitted light, or an extent of depolarization.

Many variations could be made to the embodiments of the calibration targets described above without departing from the spirit or scope of the present invention. For instance, although each of the embodiments shown in the drawing figures have a shield holder and a calibration/reference target that is generally circular or annular in shape, any other shape could be used without departing from the invention. For instance, the shield holder, infection shield and calibration target could be rectangular, square, or any other shape necessary to conform to the shape of the instrument to which the device is attached.

Also, the calibration layers of the embodiments described above could have any type of optical, transmissive or fluorescent properties used to conduct a calibration or reference operation. As mentioned above, use of the term "calibration target" in the specification and claims is intended to encompass both calibration targets and reference targets. Likewise, use of the term "calibration operation" is intended to encompass both calibration and reference operations.

- In any one embodiment of the invention, the calibration layer would have very specific reflective, transmissive and/or fluorescent properties. However, calibration/reference targets embodying the invention might include different types of calibration layers having different reflective/transmissive/fluorescent properties.
- 5 For instance, colored calibration targets could be provided in a variety of different skin tones. A calibration device embodying the invention could then be selected by a user based on a patient's skin tone or age, and the selected calibration target could be used to calibrate an instrument.
- Also, the reflective/transmissive/fluorescent properties of a calibration target may be selected such that a measuring instrument can be calibrated/referenced at the mean or the median of the expected measurement range. Such a strategy will provide maximum measurement accuracy since any error is at a minimum for measurements closest to the calibration value. For example, the reflectance of a calibration target can be formulated such that its reflectance matches the median reflectance of the patients expected to be measured with the instrument. As an additional example, the fluorescence lifetime and/or quantum yield of a fluorescent target may be selected such that it equals the median lifetime and/or quantum yield of the fluorescing analyte being measured.
- 20 Also, although each of the embodiments described above have a user graspable tab attached to the calibration layer, other types of user graspable tab configurations are possible. For instance, instead of being a tab, a cord, a string or a ring of material

could be attached to the calibration layer. For instance, in the embodiment shown in Figure 18, the user graspable tab 202a is a loop of material whose ends are attached to the calibration layer 200. Each of these items is easy for the finger of a user to grasp and to pull. The invention is intended to include any type of user graspable tab, cord, string, ring, or other device that can be used to remove the calibration layer from the remaining portions of the device.

Furthermore, in the embodiments described above, an infection shield and a calibration target are attached to a shield holder, which in turn is attached to the instrument. Some embodiments of the device may not utilize a shield holder. In these embodiments, the infection shield and/or the calibration target may be directly attached to a measuring instrument. These embodiments may use an adhesive layer or a mechanical attachment device to attach the infection shield and the calibration target to the instrument.

Still further, if the instrument which the device is used with is not used for medical purposes, and infection or cross-contamination is not an issue, a device embodying the invention may simply comprise a calibration layer. The calibration target in Figure 8 provides an example of such an embodiment. This calibration target could be directly attached to the measuring instrument.

In yet another embodiment of the invention, a plurality of emitter and detector pairs could be arranged in an array on a measuring instrument. During a calibration operation using any of the calibration devices described above, the light

output from the emitters could reflect/scatter from or be transmitted through portions of the calibration device and impinge on the respective detectors. If a fluorescent calibration target is used, fluorescent light from the target could impinge on the detectors. After the calibration operation is conducted, the same emitter/detector pairs could be used to interrogate multiple points on a target material or tissue. Such a configuration would allow the measuring instrument to develop an image of the target material or tissue, or an image of reflective/transmissive/fluorescent properties of the target.

In still other embodiments, one or more light sources could illuminate/excite a target material or tissue, and reflected/scattered/transmitted light, or fluorescent light, passing from the target material or tissue could impinge on a detector array configured generate an image of the material or tissue, or an image of the reflective/transmissive/fluorescent properties of the target material or tissue. For instance, a charged coupled device (CCD) could be used as the detector array. The calibration devices described above could be used to calibrate or reference a measuring instrument that utilizes such a detector array.

Figures 25A, 25B, and 25C show front, side and back views, respectively, of a measurement system 803 embodying the invention. Figure 25D shows the measurement system 803 in a charging stand 871. The elements in the measurement system 803 which have similar counterparts in the previously discussed system 3, will also have the earlier reference numbers indicated in parenthesis.

The measurement system 803 includes a housing 843 which is sized so as to be easily graspable by a human hand. A radiation analyzer 810 is coupled to the calibration device 845 via one or more optical fibers 833 (see Figure 25B). A calibration device 845 may be inserted into an opening end 846 of a cone-shaped holder 858 of the housing 843. A curved portion 866 of the housing 843 allows the user's hand to comfortably hold the measurement system 803.

Figure 8B shows a side view of the measurement system 803, including the radiation analyzer 810 and a push button 861. The radiation analyzer 810 is mounted on a printed circuit board (PCB) 818, which is powered by batteries 822. The batteries 822 can be recharged when the system 803 is placed in a power adapter stand through a charger connection 826. A liquid crystal display (LCD) device 832 is also coupled to the PCB 818. An LCD device 832, which is visible through a window 841, displays measurement results, instructions, warnings, and other operating information. The radiation analyzer 810 is controlled by a processor also mounted on PCB 818.

Figures 25C and 25D show a back view of system 803, which includes back portion 891 and the LCD device 832. A person can initiate a calibration, and then a measurement, by pressing push button 861 with his or her thumb. In particular, once a calibration measurement has been performed, the user graspable tab 280 (see previous figures) is used to peel the calibration target 270 away from the window 260, and the system 803 is ready to make a measurement on a patient. The LCD device

832 indicates when the measurement system 803 is ready to make a calibration measurement, when a calibration measurement has been completed and the system 803 is ready to make an actual measurement, and when the system 803 has completed a measurement. The LCD device 832 also displays the results of measurements, and messages or other indicators. For instance, the LCD device 832 might show that a particular calibration target 270 has already been used and that no additional measurements can be made until a new calibration measurement is made.

A limit switch (not shown) may be installed at the end of the tip 858 to detect the presence of a calibration device 45. Once the limit switch is engaged, a calibration measurement is enabled and a measurement counter is initialized to zero. Calibration is then performed to ready the device for taking a measurement. The system software then increments the counter each time a measurement is made, up to a predetermined maximum. Once the maximum number of measurements is reached, the system software indicates that a calibration is again required, and the device is prevented from taking additional measurements. Should the limit switch be disengaged at any time in the measurement sequence, indicating the removal of the disposable tip, the display indicates that a new calibration sequence must be begun before other measurements may be taken. These software controls prevent an operator from using one calibration target more than a predetermined number of times before replacing the calibration device.

Figure 25D shows a measurement system 803 with a charging stand 871 for storing and charging the system 803. The charging stand 871 includes a center portion 873 for receiving the system 803. The center portion 873 serves as both a stand and a recharging unit. The stand 871 has an electrical cord (not shown) which can be plugged into an outlet. The stand 871 also includes an electrical receiving unit which receives charger connection 826 (see Figure 8B) of the system 803. An indicator light 876 indicates when the measurement system 803 is properly placed in the center portion 873 so that recharging may take place. The stand 871 further includes a side receiving portion 875 which can be used to hold a supply 877 of calibration devices 845.

A measuring instrument embodying the invention to transmit measurement data directly from the instrument to a recording device via a wireless communication system. The wireless communication system could be a radio link or infrared communication link. Similarly, a charger stand for the measurement instrument could receive measurement data and transmit the measurement data to a recording device via a communication link.

Figure 26A is a schematic diagram of certain elements of a measurement system 803, and in particular, of a radiation analyzer instrument 810. The radiation analyzing instrument 810 includes an optical unit 914, a central processor unit (CPU) 905, and a memory 909. Figure 26B shows a perspective view of an optical unit 914 that includes an optical source 918, a detector array 923, an optical grating 951 and

an output 955 which couples the optical unit 914 to the CPU 905 via a data bus 961. The optical source 918 may be a tungsten halogen bulb, a noble gas filled tungsten bulb or several LED's covering the desired regions of the optical spectrum. The optical source 918 may also be placed at a location in the device housing to illuminate the subject directly, without coupling the radiation into a fiber.

The embodiment shown in Figure 26B utilizes a microspectrometer offered by American Laubscher Corporation of Farmingdale, LI, NY called the VIS/NIR microspectrometer. Optical radiation 940 is output from optical source 918 and is transmitted via fiber 833 to the target (not shown) to be measured. The return signal 941 travels back down optical fiber 833 and is output from fiber end 958 into a type of waveguide 962 (cut away) and is incident on diffraction grating 951. Diffraction grating 951 achieves self-focussing of radiation 941 to different points or detectors on diode array 923, depending on the intensity and wavelengths of the return radiation 941.

The operation of system 803 will now be described in conjunction with Figures 26A and 26B. First, a calibration target starts out being arranged on a window of the measuring system, and a user pushes a button, which indicates that a calibration measurement should be taken. Radiation 940 is emitted toward the calibration target, which reflects at least a portion of the radiation back to the measurement system. Because the calibration target has a known spectral characteristic, the returned radiation 941 results in a detected intensity at individual

detectors on the detector array 923, thereby yielding a measured calibration characteristic. This measured calibration characteristic is compared to the expected or known spectral characteristic of the calibration target, and a resulting adjustment value (which could be an array of values) is determined. The calibration target is then removed, and a measurement of tissue or material is made by outputting radiation 940 as above. A resulting spectral characteristic is then output from detector array 923, which in turn is adjusted by CPU 905 using the adjustment value or characteristic to yield a calibrated spectral characteristic. The calibrated spectral characteristic can then be used to determine some measurable characteristic of the material or tissue. One such measurement is a non-intrusive bilirubin measurement according to one embodiment of the invention, as will be discussed below.

Although a microspectrometer as shown in Figure 26B may be used in an embodiment of the invention, other devices capable of measuring the amplitude of radiation reflected from a patient's skin at different wavelengths can also be used. For instance, Figure 31 shows a radiation analyzing device that includes a processor 905, a radiation source 918, radiation conduits 833, such as optical fibers, a memory 909 and a filter/detector unit 1000. The filter/detector unit may comprise a plurality of detectors and filters. For instance, filters 1, 2 and 3 1010, 1020 and 1030, may be designed to pass only discreet wavelengths of the radiation reflected from a patient's skin. Each of the filters may be paired with a corresponding detector to determine the amplitude of light reflected from a patient's skin at each of the three filter

wavelengths. Alternatively, the filters may be successively coupled to a single detector to determine the amplitude of the reflected light at each of the filter wavelengths. In yet another embodiment, the filter/detector unit 1000 may comprise a detector with a linear variable filter.

5 If the radiation conduits 833 of the device shown in Figure 31 comprise optical fibers, the numerical aperture of the optical fibers can be selected to optimize the efficiency of the device. For instance, the optical fibers used to transmit radiation from the radiation source 918 to the patient's skin may have a numerical aperture matched to the radiation source 918. In addition, the optical fibers used to transmit 10 light reflected from the patient's skin to the radiation analyzer may have a numerical aperture matched to the radiation analyzer.

The optical fiber 833 of measurement device 803 may comprise one or a plurality of fibers. Preferably, the optical fiber 833 comprises a plurality of fibers arranged in a bundle. Figure 27 shows a bundle of optical fibers 333 which can be used to transmit and receive radiation. The optical fibers are arranged so that they approach a surface of a material or tissue 40 to be measured at an angle θ relative to an axis perpendicular to the surface of the material or tissue 40. When the bundle of optical fibers is inclined in this manner, backscattering effects are reduced. Angle θ is preferably not 0° and sufficiently large to prevent backscattering effects. In one embodiment, angle θ is between a few degrees and 20° and preferably between 5° and 15 10° and more preferably approximately 7° .
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Figure 28 shows the bundle of optical fibers 333 as seen from section line 28-28 of Figure 27. In the bundle of optical fibers 333, there is an outer ring of transmission optical fibers 336, an inner ring of transmission fibers 337 and a central receive optical fiber 335. When the device is in operation, radiation is transmitted through the first and second rings of transmission fibers 336, 337, is reflected off the skin of a patient, and received by the receive optical fiber 335.

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Figure 29 shows the bundle of optical fibers as seen from section line 29-29 of Figure 27. Because the ends of the optical fibers are cut at a slight angle, and because the optical fibers themselves are cylindrical, the ends of the optical fibers appear to be ovals in Figure 29.

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Figure 30 shows a receive optical fiber 335 and four transmit optical fibers 336 and 337 surrounding the receive optical fiber 335. The receive optical fiber has a smaller numerical aperture than the transmit optical fibers. The lines extending down from the bottom of the optical fibers show the path that radiation would take to leave or enter the optical fibers. For instance the area 335A shows the path that radiation may take to enter the receive optical fiber 335. The areas marked 336A and 337A show the path that radiation may take when leaving a transmit optical fiber 336 and 337. Typically, the numerical aperture of the receive optical fiber 335 will be smaller than the numerical aperture of the transmit optical fibers 336 and 337.

Bilirubin Measurement Process

U.S. Patent No. 5,353,790, the contents of which are incorporated herein by reference, presents a method and apparatus for determining bilirubin concentration in human tissue such as skin. In particular, the patent discusses reflecting light from the skin of a patient to determine a bilirubin concentration. The approach corrects for maturity-dependent optical properties of the skin, including the amount of melanin in the skin and the amount of blood in the skin. Reflected red to infrared light is used to determine the maturity-dependent optical properties, reflected red light is used to determine melanin content, and reflected yellow-orange light is used to determine the amount of blood in the skin. These quantities are used, in combination with reflected blue light, to calculate cutaneous bilirubin concentration.

U.S. Patent No. 5,353,790 discusses the absorption spectrum of melanin and shows that the melanin absorption spectra essentially decreases linearly with wavelength in the visible region. Moreover, since the melanin absorption varies orders of magnitudes over the visible region, variations in skin pigmentation will cause large absolute changes in the absorption at the shorter wavelengths, but the same magnitude changes will cause relatively minuscule absolute changes in the very long wavelengths (> 800 nm). The melanin pigmentation measured in the far red wavelength range was found to have a pivot point at around 637 nm.

A measurement system embodying the invention and configured to detect a bilirubin concentration in a patient takes advantage of the above phenomena and uses

spectral reflectance to determine a serum bilirubin level in mg/dL (milligrams of bilirubin per deciliters of blood), as will now be discussed. Figure 32 shows a flowchart setting forth the steps of a first method embodying the invention that may be used by a measurement system to perform bilirubin measurements on a patient.

5 The steps performed are an improved version of the approach discussed in U.S. Patent No. 5,353,790. Step 702 involves performing a calibration measurement in a manner similar to that described above. This involves simply outputting radiation to a calibration target, and measuring the return signal (which could be reflected/scattered/transmitted/ flourescent light). The calibration measurement yields a measured calibration spectrum, which is compared to an expected calibration spectrum (which in turn, depends on the calibration target). The difference between the expected or known spectrum and the measured spectrum serves as the calibration data. The calibration data is used to modify actual measured data, thereby compensating for unit to unit and time varying changes in source luminosity, delivery optics, collection optics, detection sensitivity, electronic drift, and environmental conditions such as temperature and humidity.

10 15

Step 704 involves making a measurement of a patient's skin by illuminating the skin with light and detecting a frequency spectrum of light reflected from the patient's skin. Step 708 involves converting the reflection (scattering) measurements into an optical density. Step 712 then involves calculating, from a first portion of the spectrum, a first parameter indicative of a maturity of the skin. Step 716 involves

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calculating, from a second portion of the spectrum, a second parameter indicative of an amount of melanin in the skin. Step 720 involves calculating, from a third portion of the spectrum, a third parameter indicative of a blood content of the skin. Step 724 involves calculating, from a fourth portion of the spectrum, a fourth parameter indicative of an uncorrected bilirubin concentration in the skin. Step 728 involves calculating a corrected bilirubin concentration in the skin as a function of the first, second, third and fourth parameters.

Figure 33 shows the results of data taken using the method illustrated in Figure 32, versus a standard serum bilirubin (heel stick) method. The subjects were 72 full term babies of varied ethnic background, with 20 African Americans, 2 Hispanic Americans, 48 white Americans, and 2 Asian Americans. "R" represents the correlation coefficient between the measurement method described in Figure 32, versus the standard method of serum bilirubin. The correlation coefficient shown is 0.9165 with a perfect correlation given as 1.0000. The tests represent a purely prospective application of the method illustrated in Figure 32.

Figure 34 shows a flowchart setting forth the steps of another method embodying the invention for measuring a bilirubin concentration of a patient. This second method is a more simplified method compared to the method described above. In step 1805 the measurement system first makes a calibration measurement as described above. Next, in step 1810, a measurement is made using a first portion of the spectrum to determine an amplitude of the reflected light at a first wavelength.

Next, in step 1815, a measurement is made at a second portion of the spectrum to determine an amplitude of light at a second wavelength. The first and second wavelengths are indicative of the blood content of the patient's skin. In step 1820, a third measurement is made to determine the amplitude of the reflective light at a 5 third wavelength indicative of an uncorrected bilirubin score. In step 1825, a CPU of the measurement device calculates a calibrated and corrected bilirubin concentration using the results of steps 1805 through 1820.

The significance of making measurements at the first and second wavelengths will now be explained with reference to Figure 35. Figure 35 illustrates two lines, L3 10 and L4, that represent the amplitude of light reflected from a patient's skin under two different conditions. In a first condition, the blood flowing through the patient's skin is fully oxygenated. In the second condition, the blood flowing through the patient's skin has no oxygen attached to the hemoglobin in the blood. As shown in Figure 35, lines L3 and L4 cross one another at two points H and I. Experimental 15 results have indicated that the wavelengths corresponding to points H and I are at approximately 526 and 585 nanometers, respectively.

By making the measurements of the amplitude of light reflected from a patient's skin at approximately 526 nanometers and 586 nanometers, it is possible to obtain a measurement representative of the blood content of the patient's skin. 20 Because the measurements are made at the crossover points, it does not matter whether the blood in the patient's skin is fully or partially oxygenated.

The method of calculating a calibrated and corrected bilirubin concentration of Figure 34 will now be further explained with reference to Figure 36. In Figure 36, L5 represents an amplitude of light reflected from a patient's skin at various wavelengths.

5 The amplitude of light reflected from a patient's skin at a first wavelength, as measured in step 1810, is taken at a wavelength of approximately 526 nanometers. The amplitude at this wavelength is represented by point B in Figure 16. The amplitude of the light reflected from the patient's skin at the second wavelength is taken at approximately 586 nanometers, which is represented by point C in Figure
10 36. An imaginary line L1 is drawn through points B and C and backwards through smaller wavelengths of the visible light spectrum. The amplitude value at the intersection of the line L1 and an imaginary line at 476 nanometers is then determined, which is represented by point D in Figure 36. Point A in Figure 36 represents the measured amplitude of the light reflected from the patient's skin at 476
15 nanometers. The value of point D is then subtracted from the value of point A to determine a corrected bilirubin score. This corrected bilirubin score is then used with the calibration data taken during a calibration measurement to determine a calibrated and corrected bilirubin concentration of the patient's skin.

20 The second method described above is far more simple than the first method, as it only involves taking amplitude measurements of reflected light at three discreet wavelengths. Experimental results have shown that the second method provides

substantially the same level of accuracy as the first method, and in some cases the second method produces even better results.

A third method of determining a bilirubin concentration in a patient's skin will now be described with reference to Figure 37. Figure 37 shows a flowchart of the steps of a third method of determining a patient's bilirubin concentration. In step 1905, a calibration measurement is taken as described above. In step 1910, measurements of the amplitude of light reflected from a patient's skin are made at first, second, third, fourth and fifth wavelengths. In step 1915, the first, second and third measurements are adjusted based on the fourth and fifth measurements. In step 1920, a calibrated and corrected bilirubin concentration is calculated using the calibration measurement and the adjusted first, second and third measurements:

The first, second and third measurements taken during step 1910 are taken at the wavelengths 486 nanometers, 526 nanometers, and 586 nanometers as described above in connection with the second method. The fourth and fifth measurements are taken at wavelengths J and K, as shown in Figure 36, which are represented by the points M and N. The wavelengths corresponding to J and K are in the range between 600 and 700 nanometers. The amplitude of the light reflected from the patient's skin at frequencies J and K are representative of melanin in the patient's skin. A line drawn through points J and K will have a negative slope that indicates the amount of melanin in the patient's skin. The greater than negative slope (or the

more steeply the line is inclined down toward the right) the greater the amount of melanin.

In step 1915, the first, second and third measurements are adjusted based on the fourth and fifth measurements. To accomplish this adjustment, a line L2 is drawn through points M and N, and the line L2 is projected backwards through the smaller wavelengths, as shown in Figure 36. Points of intersection of the line L2 with imaginary lines at the first, second and third wavelengths are determined. These points are shown as points E, F and G in Figure 36. The amplitude values of points E, F and G are then subtracted from the respective measurements made at these wavelengths, which are shown as points C, B and A. These adjusted measurements for the first, second and third wavelengths are then used to determine a calibrated and corrected bilirubin concentration for the patient according to the methods described above.

The above-described process calls for a single measurement to be made on a single location on a patient's skin. A measuring device embodying the invention could be configured to take a plurality of measurements on the same portion of the patient's body, or at different portions of the patient's body and to average the measurements to create a final measurement result. Also, if a plurality of measurements are taken, one or more of the measurements having the greatest deviation may be discarded, and an average of a lesser number of measurements may be created to arrive at a final measurement result. Further, if the deviation between

a plurality of measurements exceeds a predetermined standard deviation, the entire set of measurements may be discarded, and a new set of measurements may be obtained.

Many alternatives and modifications of the above examples would be apparent to those skilled in the art upon reading the foregoing or practicing the invention. The apparatus and methods described above are intended to be exemplary and are not intended to limit the scope of the invention as defined by the following claims.

WHAT IS CLAIMED IS:

1. A disposable calibration device, comprising:
 - a double-sided adhesive layer, wherein an adhesive strength on a first side of the adhesive layer is greater than an adhesive strength on a second side of the adhesive layer; and
 - 5 a calibration target arranged on at least one side of the adhesive layer.
2. The device of claim 1, wherein the calibration target is arranged on the first side of the adhesive layer.
3. The device of claim 1, wherein the calibration target includes a user graspable tab.
4. The device of claim 1, wherein the calibration target includes a reduced strength portion, and wherein the calibration target will tear or separate along the reduced strength portion when the calibration target is separated from other portions of the calibration device.
5. The device of claim 4, wherein the reduced strength portion comprises at least one of a slit, a perforation, and a crease.

6. The device of claim 1, wherein the calibration target is configured such that the calibration target will tear or separate in a predetermined manner when the calibration target is removed from other portions of the calibration device.
7. The device of claim 1, further comprising a cutter for causing the calibration target to tear or separate in a predetermined manner when the calibration target is removed from other portions of the calibration device.
8. The device of claim 7, wherein the cutter comprises one of a wire or a monofilament.
9. The device of claim 1, wherein the double-sided adhesive layer extends around all but a portion of a peripheral edge of the calibration target.
10. The device of claim 1, wherein the calibration target includes a calibration portion having properties that are usable for calibration or reference of an instrument to which the calibration device is attached.

11. The device of claim 10, wherein the calibration target further comprises a reduced strength portion that is configured so that the calibration target tears or separates across the calibration portion when the calibration target is removed from other portions of the calibration device.

12. The device of claim 11, wherein the adhesive layer extends around all but a selected portion of a periphery of the calibration target, and wherein the calibration target and the adhesive layer are oriented with respect to one another so that the adhesive layer aids tearing or separation of the calibration target when the calibration target is removed from other portions of the calibration device.

13. The device of claim 1, further comprising a shield layer arranged on a side of the double-sided adhesive layer opposite the calibration target.

14. The device of claim 13, wherein the double-sided adhesive layer comprises a first double adhesive layer, and further comprising a second double adhesive layer arranged on a side of the shield layer opposite the double-sided adhesive layer.

15. The device of claim 14, further comprising a calibration device holder that is attachable to a measuring instrument, wherein the second double-sided adhesive layer attaches the shield layer to the calibration device holder.

16. The device of claim 1, further comprising a calibration device holder that is attachable to a measuring instrument, wherein the double-sided adhesive layer and the calibration target are removably attached to the calibration device holder.

17. The device of claim 16, wherein the calibration device holder includes a shield layer.

18. A disposable calibration device, comprising:

a calibration layer; and

means for attaching the calibration layer to a measuring instrument,
wherein the device is configured such that the calibration layer will tear or separate
5 in a predetermined manner when the calibration layer is removed from the
measuring instrument.

19. The device of claim 18, wherein the calibration layer includes a reduced strength portion that causes the calibration layer to tear or separate in a predetermined manner when the calibration layer is removed from the measuring instrument.

20. A calibration device, comprising:

a structure, through which radiation can pass; and

a removable calibration target arranged on said opening, wherein the removable calibration target includes a fluorescent portion.

21. The calibration device of claim 20, further comprising an adhesive portion configured to adhere the removable calibration target to a measuring instrument.

22. The calibration device of claim 20, wherein the removable calibration target includes at least one reduced strength portion configured such that the removable calibration target will tear or separate along the at least one reduced strength portion when the removable calibration target is removed from other portions of the calibration device.

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23. The calibration target of claim 20, further comprising a shield layer attached to the structure.
24. The calibration target of claim 23, wherein the shield layer is arranged on the structure such that when the calibration target is removed from the structure, the shield layer remains attached to the structure.
25. A calibration device, comprising:
a structure, through which radiation can pass; and
a removable calibration target arranged on said opening, wherein the removable calibration target includes a transmissive portion configured to allow a measurement instrument to conduct a calibration operation using radiation that is transmitted through the calibration target.
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26. The calibration device of claim 25, wherein the structure comprises an adhesive portion configured to adhere the removable calibration target to a measuring instrument to which the calibration device is attached.
27. The calibration device of claim 25, wherein the removable calibration target includes at least one reduced strength portion configured such that the removable calibration target will tear or separate along the at least one reduced

strength portion when the removable calibration target is removed from other
5 portions of the calibration device.

28. The calibration target of claim 25, further comprising a shield layer attached to the structure.

29. The calibration target of claim 28, wherein the shield layer is arranged on the structure such that when the calibration target is removed from the structure, the shield layer remains attached to the structure.

30. A calibration device, comprising:
a calibration target holder configured to be arranged on a measuring instrument; and
a calibration target having known optical properties that is mountable
5 on the holder.

31. The calibration device of claim 30, wherein the calibration target holder is configured to block external light from reaching a detector of a measuring instrument when the holder is arranged on a measuring instrument.

32. The calibration device of claim 30, further comprising a shield layer, wherein the calibration device is configured such that when the calibration device is arranged on a measuring instrument, and the calibration target is removed, the shield layer remains attached to the measuring instrument.

33. A calibration device for calibrating a measuring system that transmits radiation to a material or tissue from an output end to effect measurements, comprising:

a removable calibration target;

5 a structure for holding the removable calibration target, the structure including an opening through which radiation can be transmitted; and

an index matching agent for interposition between the output end of the measuring system and the material or tissue being measured.

34. The calibration device of claim 33, wherein the index matching agent comprises a window of a soft polymer that is attached to the structure.

35. The calibration device of claim 33, wherein a substance held within the structure acts an index matching agent between the output end of the measuring system and the removable calibration target while the calibration target is attached to the structure, and wherein the substance acts as an index matching agent between

5 the output end of the measuring system and a material or tissue being measured when the removable calibration target is removed.

36. A method of calibrating a measuring instrument, comprising the steps of:

arranging a fluorescent calibration device on a measuring instrument;

conducting a calibration measurement using the fluorescent calibration

5 device; and

removing at least a portion of the fluorescent calibration device from the measuring instrument.

37. The method of claim 36, wherein the removing step comprises leaving a structure of the fluorescent calibration device attached to the measuring instrument such that radiation can pass through the structure during a subsequent measuring operation.

38. The method of claim 36, wherein the step of conducting a calibration measurement comprises the steps of:

illuminating a fluorescent calibration target of the calibration device with electromagnetic radiation; and

5 measuring electromagnetic radiation passing from the fluorescent calibration target to the measuring instrument.

39. The method of claim 38, wherein the illuminating step comprises illuminating the fluorescent calibration target with electromagnetic radiation having a first wavelength range, wherein the measuring step comprises measuring electromagnetic radiation having a second wavelength range, and wherein the first
5 and second wavelength ranges are not co-extensive.

40. The method of claim 38, wherein the measuring step comprises measuring fluorescent electromagnetic radiation generated by the fluorescent calibration target.

41. The method of claim 40, wherein the measuring step further comprises measuring radiation that is scattered from the calibration target.

42. The method of claim 40, wherein the measuring step comprises measuring a time characteristic of the fluorescent electromagnetic radiation.

43. The method of claim 40, wherein the measuring step comprises measuring a polarization characteristic of the fluorescent electromagnetic radiation.

44. The method of claim 38, wherein the illuminating step comprises illuminating the fluorescent calibration target with a burst of electromagnetic radiation, and wherein the measuring step comprises measuring an amount of time required for fluorescent electromagnetic radiation produced by the fluorescent calibration target in response to the burst of illuminating electromagnetic radiation to decay below a threshold value.

5 45. The method of claim 36, wherein the step of conducting a calibration measurement comprises the steps of:

illuminating the fluorescent calibration device with amplitude modulated electromagnetic radiation;

5 measuring electromagnetic radiation passing from the fluorescent calibration device to the measuring instrument; and

determining a phase shift between the illuminating amplitude modulated electromagnetic radiation and the electromagnetic radiation passing from the fluorescent calibration device to the measuring instrument.

46. The method of claim 45, wherein the measuring step comprises measuring fluorescent electromagnetic radiation generated by a fluorescent calibration target of the fluorescent calibration device.

47. The method of claim 45, further comprises a step of determining a demodulation factor, wherein the demodulation factor represents a ratio of amplitudes of the illuminating electromagnetic radiation and the electromagnetic radiation passing from the fluorescent calibration device to the measuring instrument.

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48. The method of claim 36, wherein the step of conducting a calibration measurement comprises the steps of:

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illuminating the fluorescent calibration device with polarized electromagnetic radiation;

measuring electromagnetic radiation passing from the fluorescent calibration device to the measuring instrument; and

determining a polarization difference between the illuminating electromagnetic radiation and the electromagnetic radiation passing from the fluorescent calibration device to the measuring instrument.

49. A method of calibrating a measuring instrument, comprising the steps of:

placing a transmissive calibration device over an output end of a measuring instrument;

5 conducting a calibration operation using the transmissive calibration
device; and

removing at least a portion of the transmissive calibration device from the measuring instrument.

50. The method of claim 49, wherein the removing step comprises leaving a structure of the transmissive calibration device attached to the measuring instrument such that radiation can pass through the structure during a subsequent measuring operation.

51. The method of claim 49, wherein the step of conducting a calibration operation comprises the steps of:

illuminating a portion of the transmissive calibration device with electromagnetic radiation; and

5 measuring electromagnetic radiation passing through the transmissive
calibration device.

52. The method of claim 51, wherein the illuminating step comprises illuminating a portion of the transmissive calibration device with electromagnetic radiation generated by the measuring instrument.

53. The method of claim 51, wherein the illuminating step comprises illuminating a portion of the transmissive calibration device with electromagnetic radiation generated by a source external to the measuring instrument.

54. A method of conducting a calibration operation, comprising the steps of:

arranging a calibration device on a measuring instrument, wherein the calibration device includes a calibration target, and wherein a portion of the calibration target has predetermined optical properties;

conducting a calibration operation using the calibration target; and

removing the calibration target from the calibration device such that the portion of the calibration target having predetermined optical properties is irrevocably altered.

55. The method of claim 54, wherein the removing step comprises at least partially destroying the portion of the calibration target having known optical properties.

56. The method of claim 54, wherein the removing step comprises removing the calibration target such that the calibration target tears or separates along a reduced strength portion.

57. A method of measuring an optical property, comprising the steps:

- attaching a reference target to a measuring instrument;
- conducting at least one reference measurement on the reference target to determine a reference value;
- conducting at least one object measurement on an object to determine an object value; and
- calculating an optical property of the object based on a relationship between the object value and the reference value.

58. The method of claim 57, wherein the step of conducting at least one reference measurement comprises:

- conducting a measurement on the reference target with a light source of the measuring instrument turned off to obtain a dark reference reading;
- conducting a measurement on the reference target with the light source of the measuring instrument turned on to obtain a reference reading; and
- subtracting the dark reference reading from the reference reading to obtain the reference value.

59. The method of claim 57, wherein the step of conducting at least one object measurement comprises:

conducting a measurement on an object with a light source of the measuring instrument turned off to obtain a dark object reading;

5 conducting a measurement on the object with a light source of the measuring instrument turned on to obtain an object reading; and

substracting the dark object reading from the object reading to obtain the object value.

60. The method of claim 57, wherein the step of calculating an optical property comprises calculating a logarithm of a ratio of the object value to the reference value.

61. The method of claim 57, wherein the step of conducting a reference measurement and the step of conducting an object measurement both comprise correcting for stray light.

62. A method of measuring a condition of a target object with a device that outputs radiation from a distal end of the device, comprising the steps of:

5 applying an index matching agent to one of the target object and the distal end of the device;

emitting radiation from the distal end of the device so that the radiation passes through the index matching agent to the target object;

receiving radiation passing from the target object to the distal end of the device; and

analyzing the received radiation to determine a condition of the target
10 object.

63. The method of claim 62, further comprising the step of conducting a calibration measurement on a calibration target and storing resulting calibration data prior to performing the emitting step.

64. The method of claim 63, wherein the step of conducting a calibration measurement comprises the steps of:

emitting radiation from the distal end of the device toward the calibration target;

5 receiving radiation passing from the calibration target to the distal end of the device; and

calculating calibration data based on the received radiation.

65. The method of claim 63, wherein the step of applying an index matching agent is performed before the calibration measurement is performed.

66. A method for determining a bilirubin concentration of a patient, comprising the steps of:

- a) illuminating a portion of a skin of the patient with light;
- b) detecting a frequency spectrum of light scattered from the skin;
- c) determining, from first and second portions of the spectrum, a first parameter indicative of a blood oxygen content of the skin;
- d) determining, from a third portion of the spectrum, a second parameter indicative of an uncorrected bilirubin concentration; and
- e) calculating a corrected bilirubin concentration based on the first and second parameters.

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70. The method of claim 66, wherein the third portion of the spectrum is at approximately 476nm.

71. The method of claim 66, wherein the performance of steps a-e result in a first corrected bilirubin concentration, and further comprising the steps of:

f) repeating steps a-e to calculate a second corrected bilirubin concentration; and

5 g) calculating an average corrected bilirubin concentration based on the first and second corrected bilirubin concentrations.

72. The method of claim 71, wherein different portions of the patient's skin are illuminated each time steps a-e are performed.

73. The method of claim 72, wherein the different portions of the patient's skin are located on different portions of the patient's body.

74. The method of claim 66, wherein the performance of steps a-e result in a first corrected bilirubin concentration, further comprising the steps of:

f) repeating steps a-e at least twice to calculate at least second and third corrected bilirubin concentrations;

- 5 g) calculating an average corrected bilirubin concentration and a standard deviation using at least the first, second and third corrected bilirubin concentrations;
- h) comparing the calculated standard deviation to a predetermined maximum standard deviation; and
- 10 i) repeating steps a-g if the calculated standard deviation exceeds the predetermined maximum standard deviation.

75. A system for determining a bilirubin concentration in a patient, comprising:

- means for illuminating a portion of the patient's skin with light;
- means for detecting a frequency spectrum of light scattered from the patient's skin;
- 5 means for determining, from first and second portions of the spectrum, a first parameter indicative of a blood content of the skin;
- means for determining, from a third portion of the spectrum, a second parameter indicative of an uncorrected bilirubin concentration; and
- 10 means for calculating a corrected bilirubin concentration based on the first and second parameters.

76. The system of claim 75, further comprising means for performing a calibration measurement on a calibration target and for storing resulting calibration data, wherein the means for calculating a corrected bilirubin concentration also utilizes the calibration data.

77. The system of claim 75, further comprising:
means for calculating an average corrected bilirubin concentration and
a standard deviation using at least three calculated corrected bilirubin concentrations;
and

5 means for comparing the calculated standard deviation to a
predetermined maximum standard deviation.

78. A system for measuring a bilirubin concentration of a patient,
comprising:

a radiation analyzing device for analyzing radiation scattered or
reflected from a patient's skin, and for outputting radiation data;

5 a radiation source;

at least one radiation transmitting conduit for conducting radiation
from the radiation source to a portion of the patient's skin;

at least one radiation receiving conduit for conducting radiation
scattered from the patient's skin to the radiation analyzing device; and

10 means for calculating a bilirubin concentration of the patient based on an amplitude of the reflected or scattered radiation at first and second wavelengths indicative of a blood content of the patient's skin and on an amplitude of the reflected or scattered radiation at a third wavelength indicative of a bilirubin concentration in the mammal's skin.

79. The system of claim 78, wherein the at least one radiation transmitting conduit directs radiation at the patient's skin at an angle relative to an axis perpendicular to the skin surface, and wherein the angle is large enough to reduce radiation backscattering.

80. The system of claim 78, further comprising a window located between the radiation transmitting and receiving conduits and an exterior measuring end of the system, wherein the window comprises a soft polymer that acts as an index matching agent between the radiation transmitting and receiving conduits and the patient's skin.
5

81. The system of claim 78, wherein the radiation analyzing device comprises a spectrometer.

82. The system of claim 78, wherein the radiation analyzing device comprises a diffraction grating and a plurality of detectors, wherein the diffraction grating focuses radiation having predetermined wavelengths on respective ones of the plurality of detectors.

83. The system of claim 78, wherein the radiation analyzing device comprises at least one radiation detector and a plurality of radiation filters, each of the plurality of radiation filters allowing only a narrow wavelength band of radiation to reach the at least one radiation detector.

84. A method for determining a bilirubin concentration of a patient, comprising the steps of:

5

- a) illuminating a portion of a skin of the patient with light;
- b) detecting a frequency spectrum of light scattered from the skin;
- c) determining, from first and second portions of the spectrum, a first parameter indicative of a blood oxygen content of the skin;
- d) determining, from third and fourth portions of the spectrum, a second parameter indicative of a melanin content of the skin;
- e) determining, from a fifth portion of the spectrum, a third parameter indicative of an uncorrected bilirubin concentration; and

10

f) calculating a corrected bilirubin concentration based on the first, second and third parameters.

85. The method of claim 84, further comprising the step of performing a calibration measurement on a calibration target and storing resulting calibration data prior to illuminating the patient's skin with light, wherein the step of calculating a corrected bilirubin concentration is also based on the calibration data.

86. The method of claim 84, wherein the first and second portions of the spectrum are at approximately 526nm and 586nm, respectively.

87. The method of claim 84, wherein the fifth portion of the spectrum is at approximately 476nm.

88. The method of claim 84, wherein the third and fourth portions of the spectrum are between approximately 600nm and approximately 700nm.

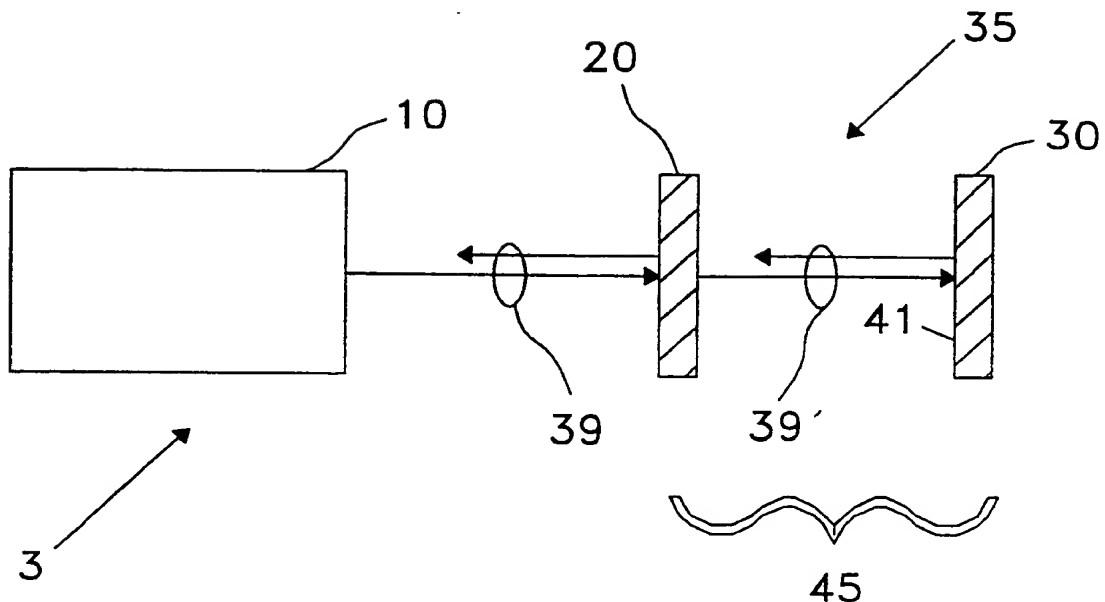


FIG. 1A

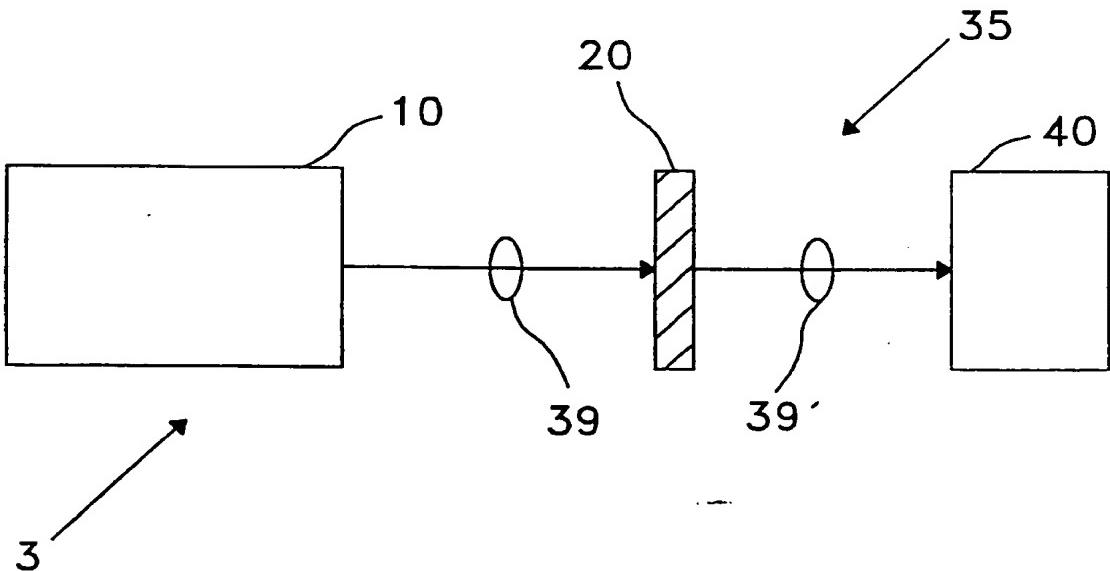


FIG. 1B

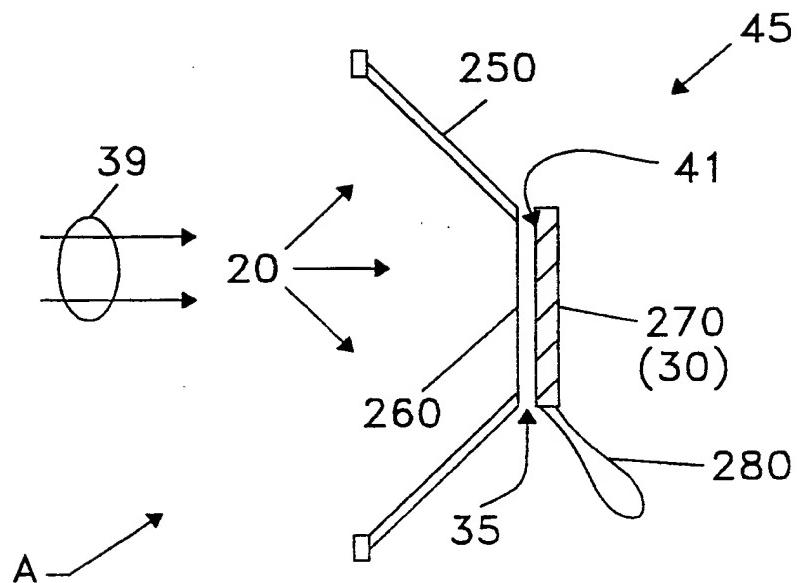


FIG. 2A

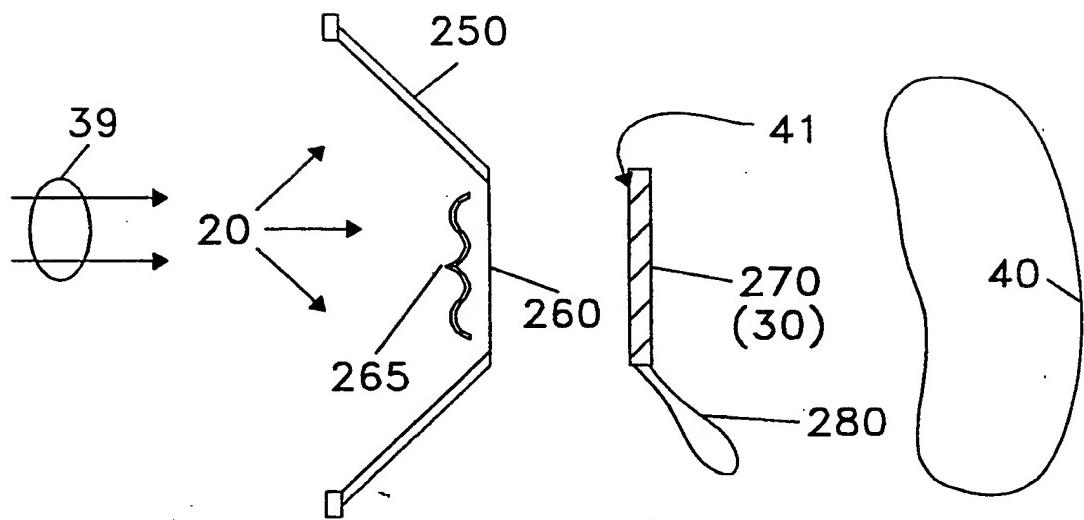


FIG. 2B

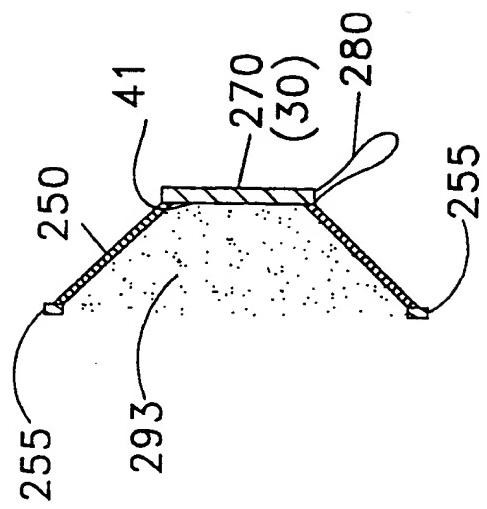


FIG. 2D

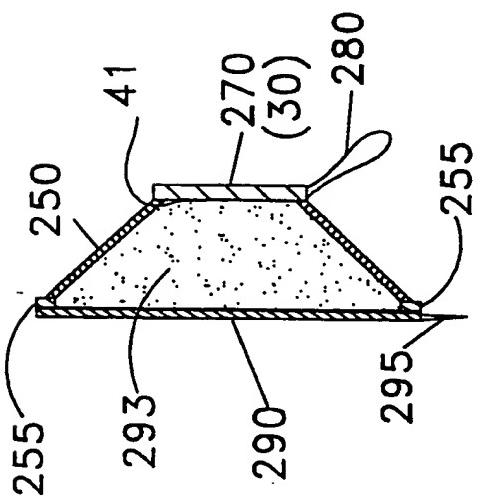


FIG. 2C

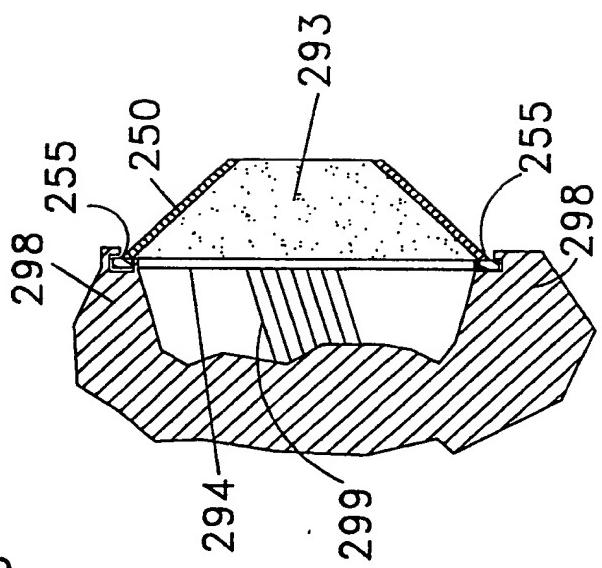


FIG. 2E

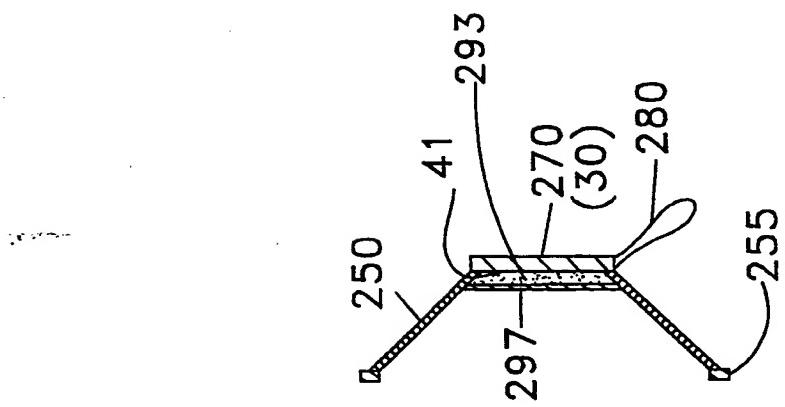
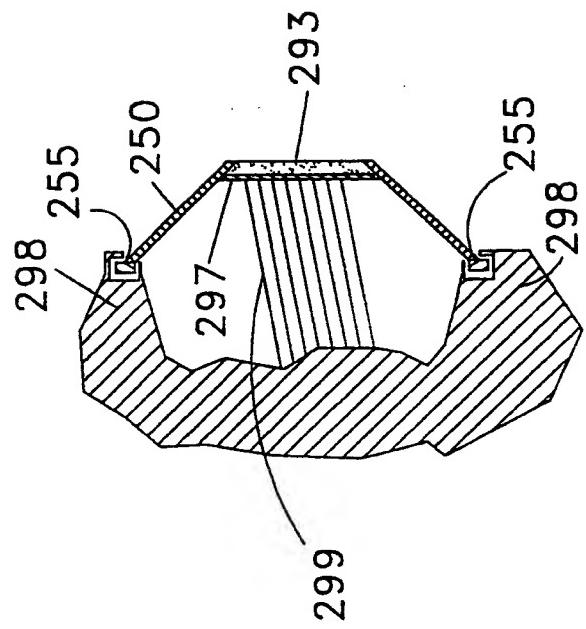


FIG. 2G

FIG. 2F

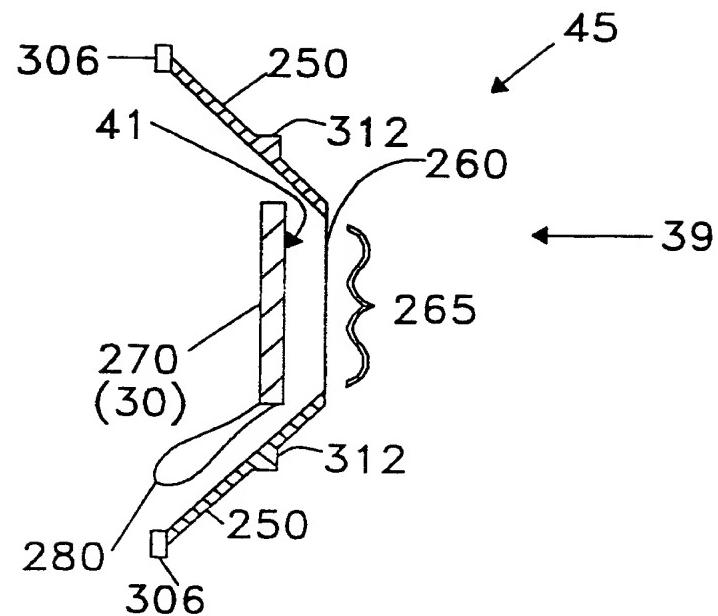


FIG. 3A

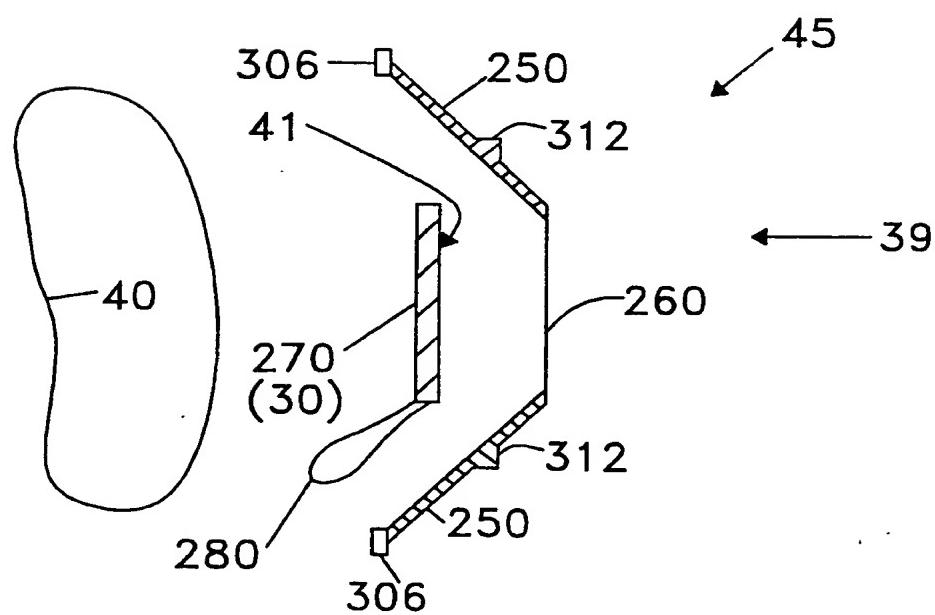


FIG. 3B

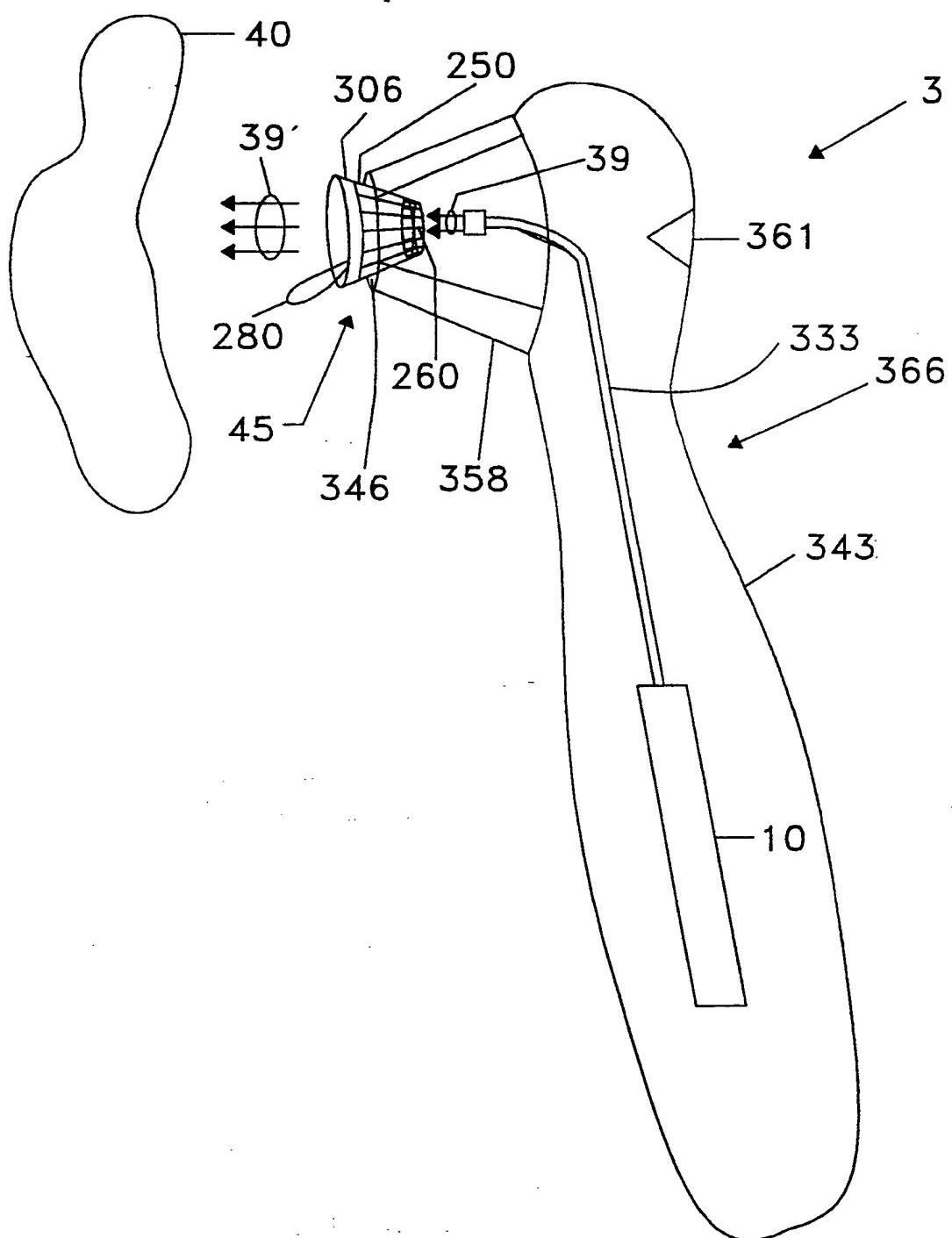


FIG. 3C

SUBSTITUTE SHEET (RULE 26)

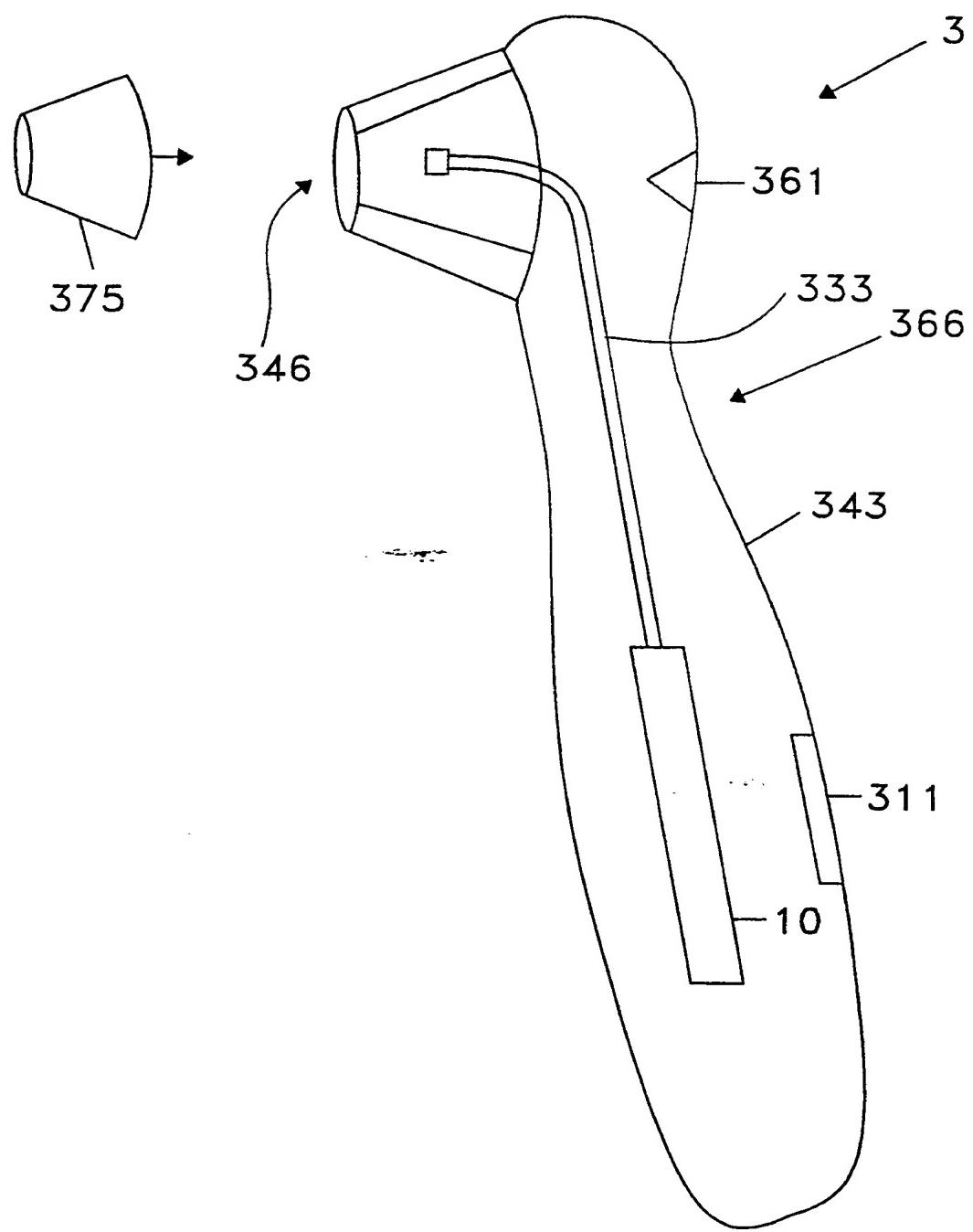


FIG. 3D

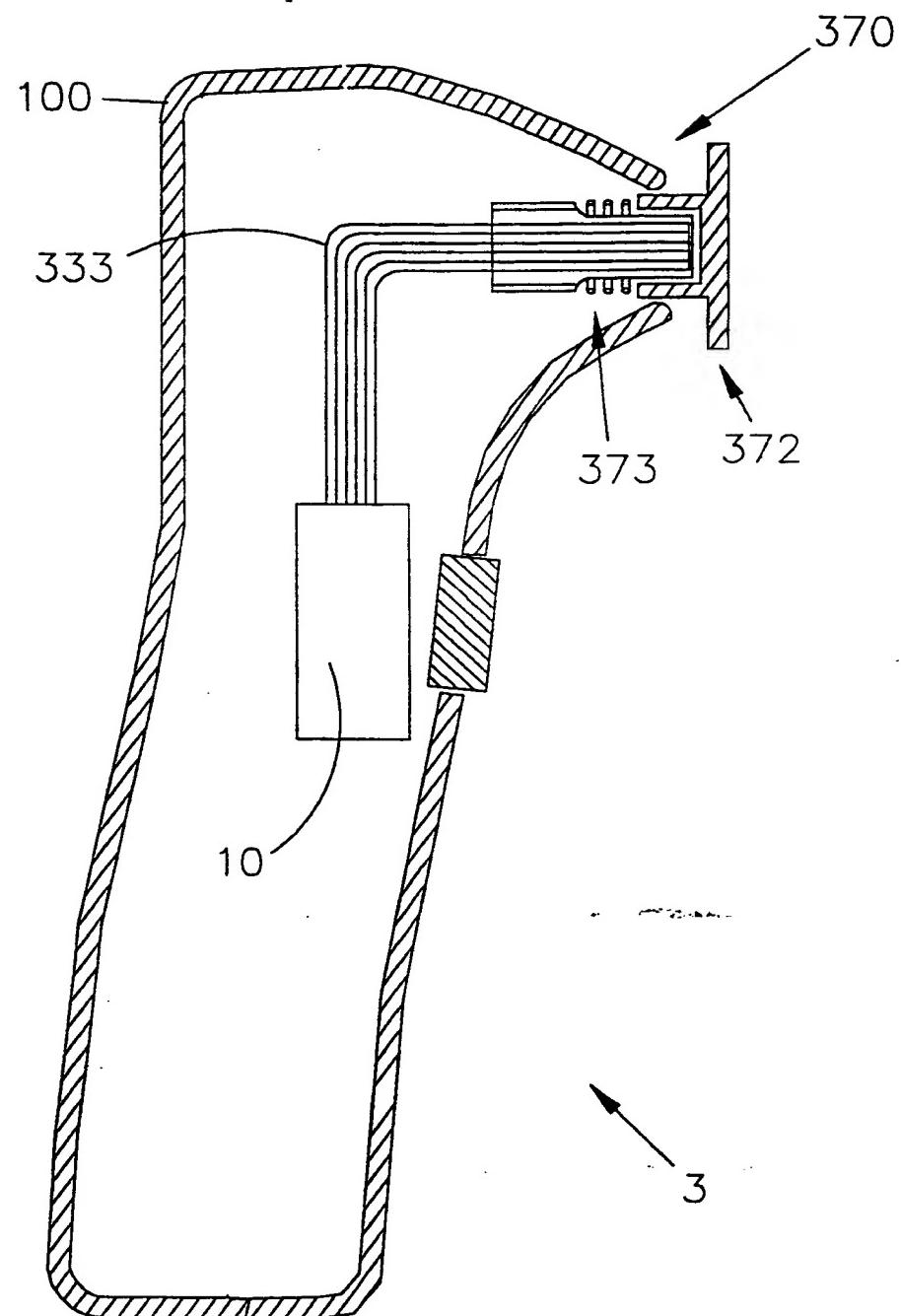


FIG. 3E

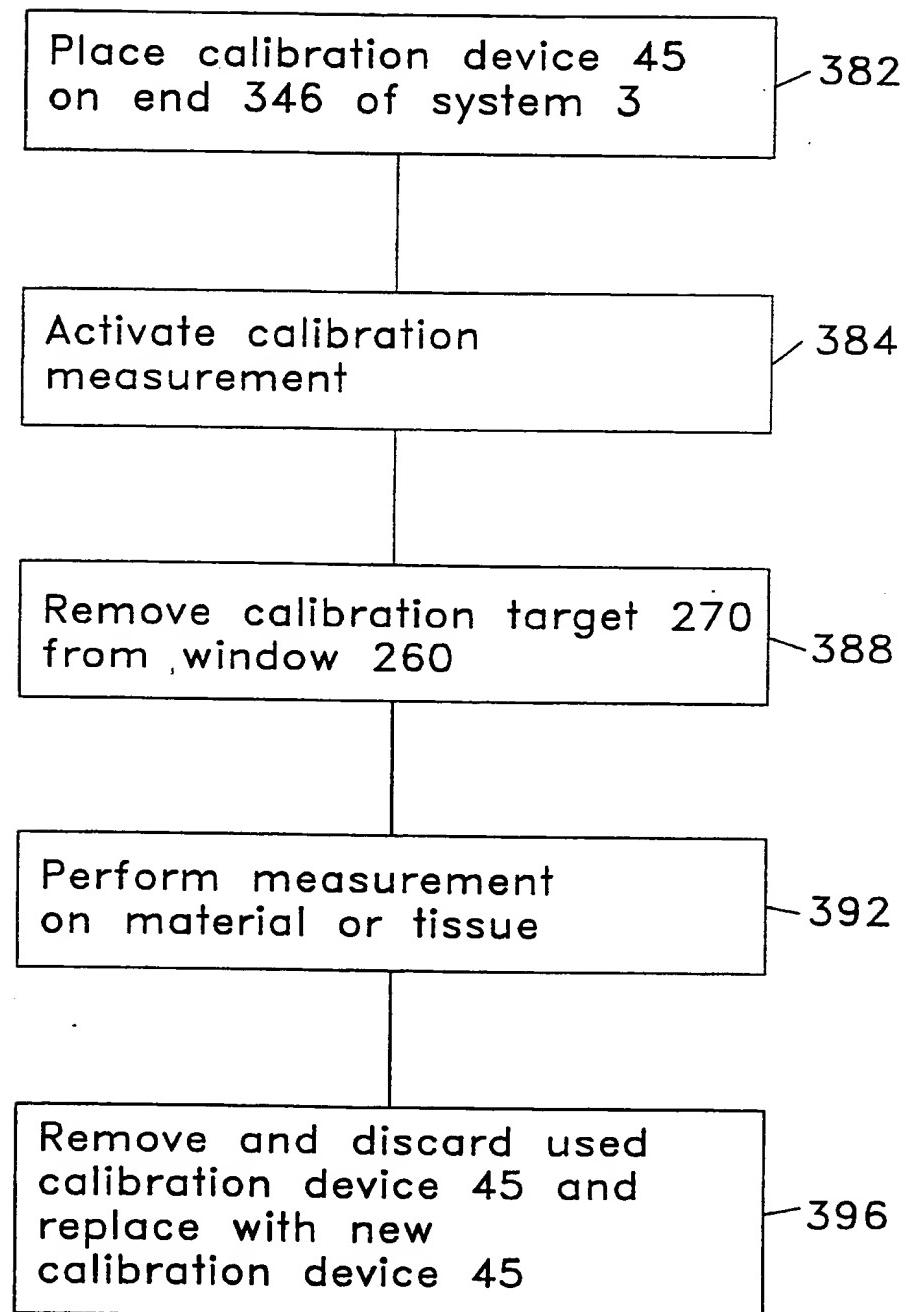


FIG. 3F

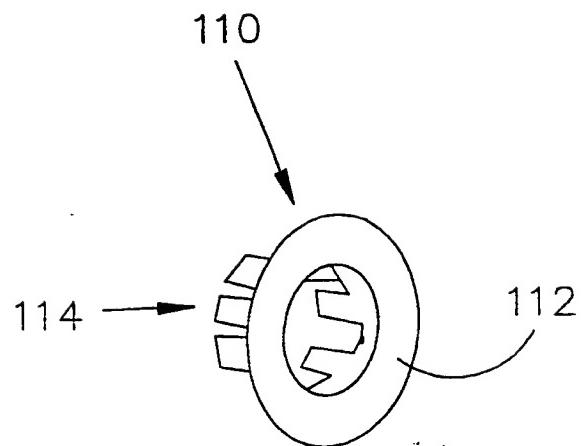


FIG. 4

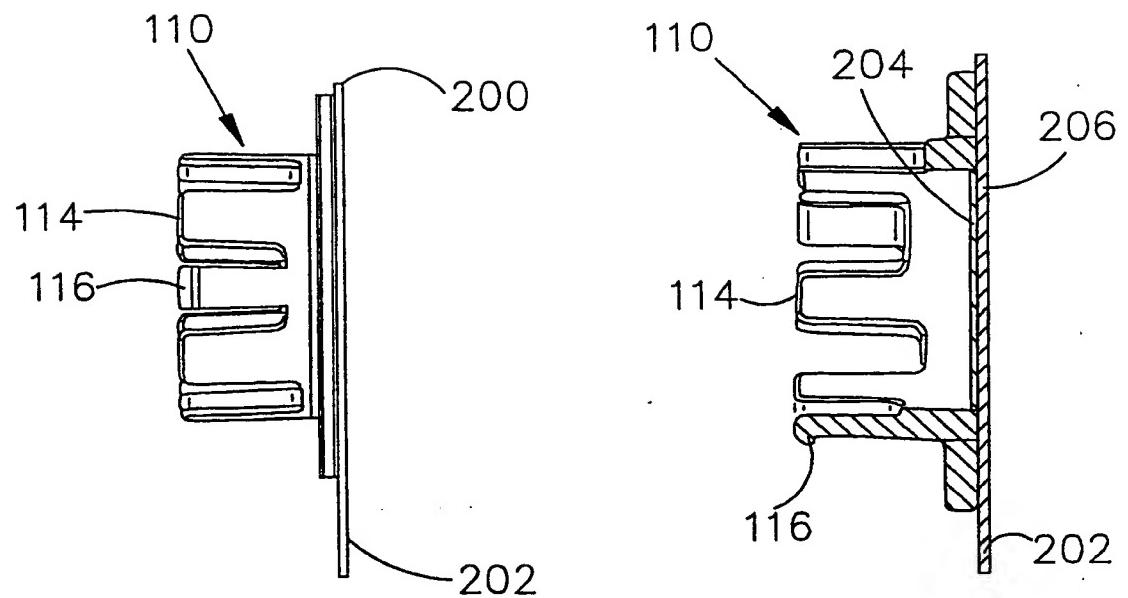


FIG. 5A

FIG. 5B

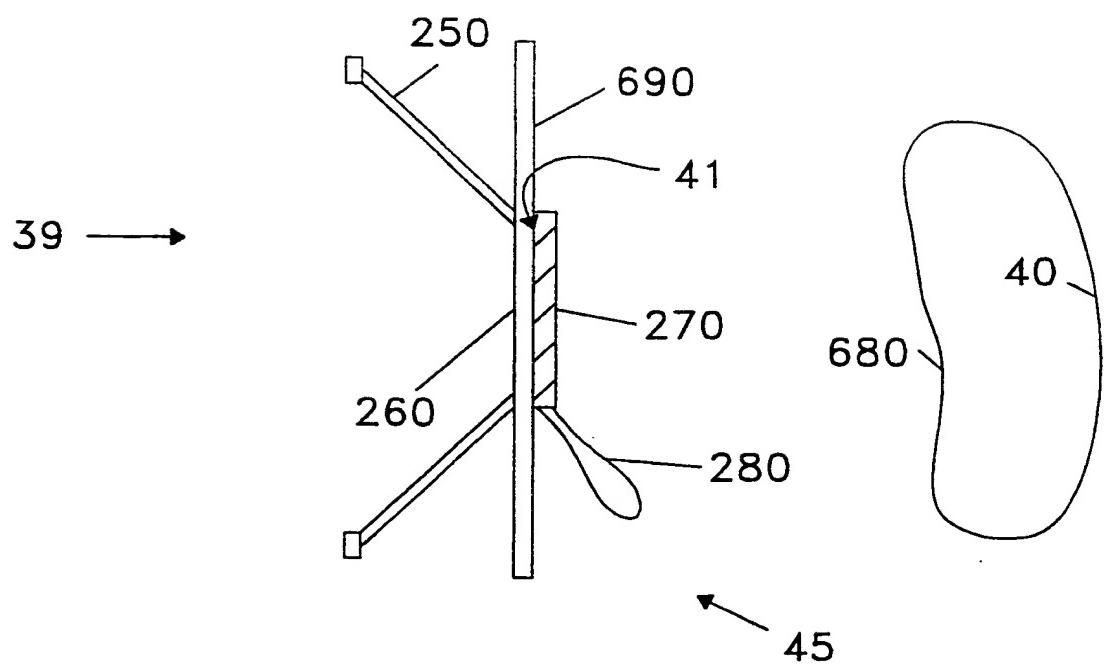


FIG. 6

SUBSTITUTE SHEET (RULE 26)

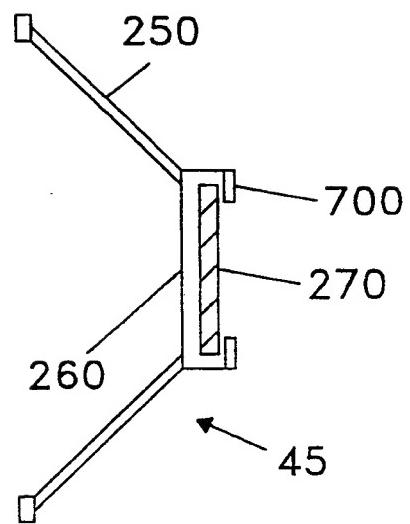


FIG. 7A

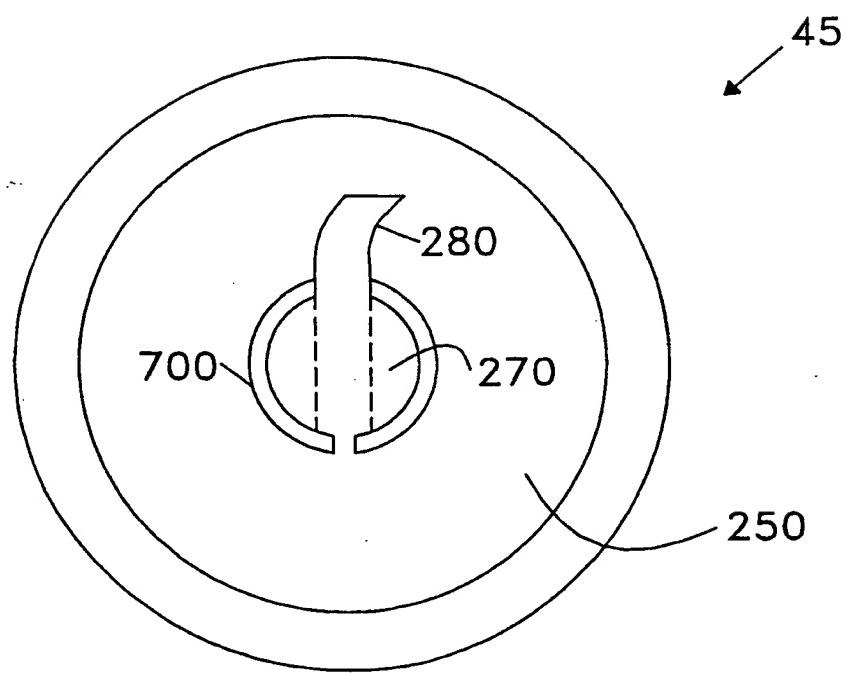


FIG. 7B

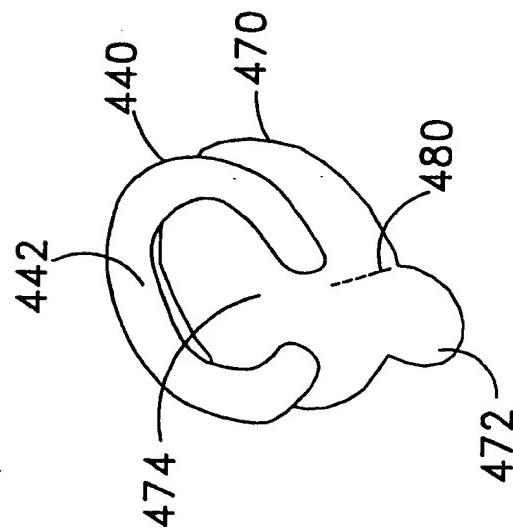
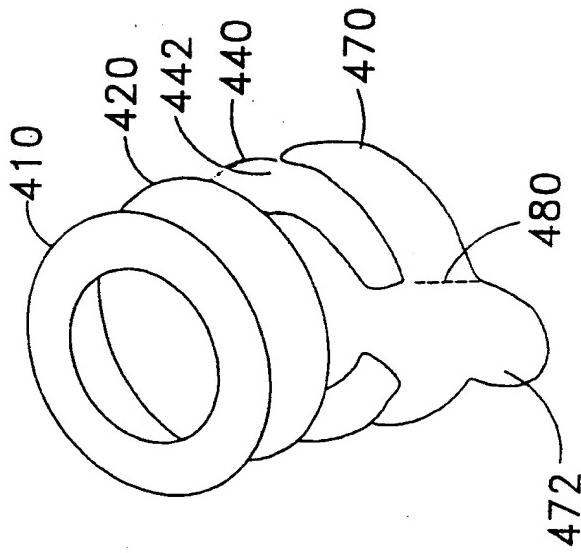


FIG. 8

FIG. 9

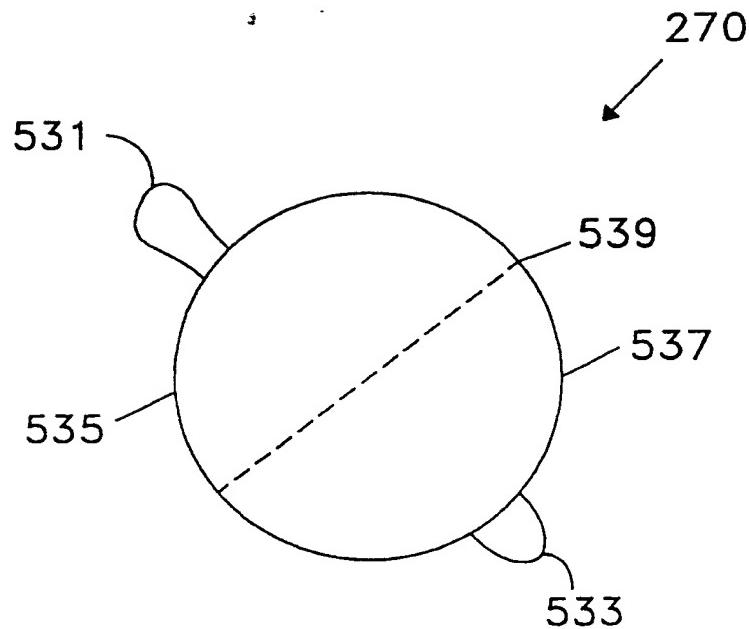


FIG. 10

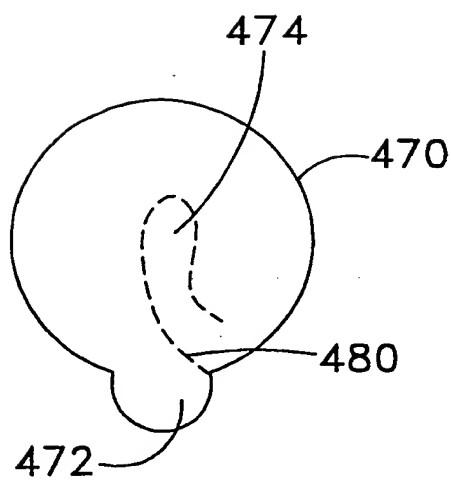
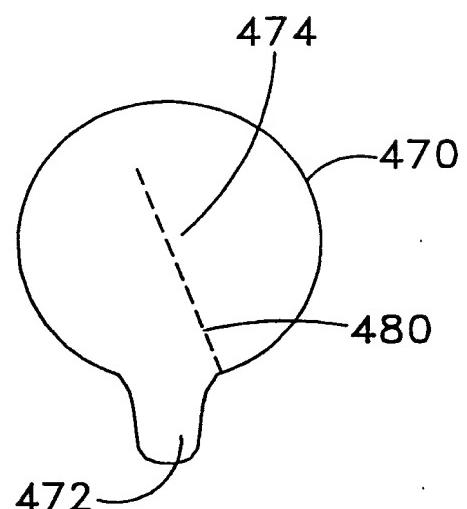


FIG. 11



SUBSTITUTE SHEET (RULE 26)

FIG. 12

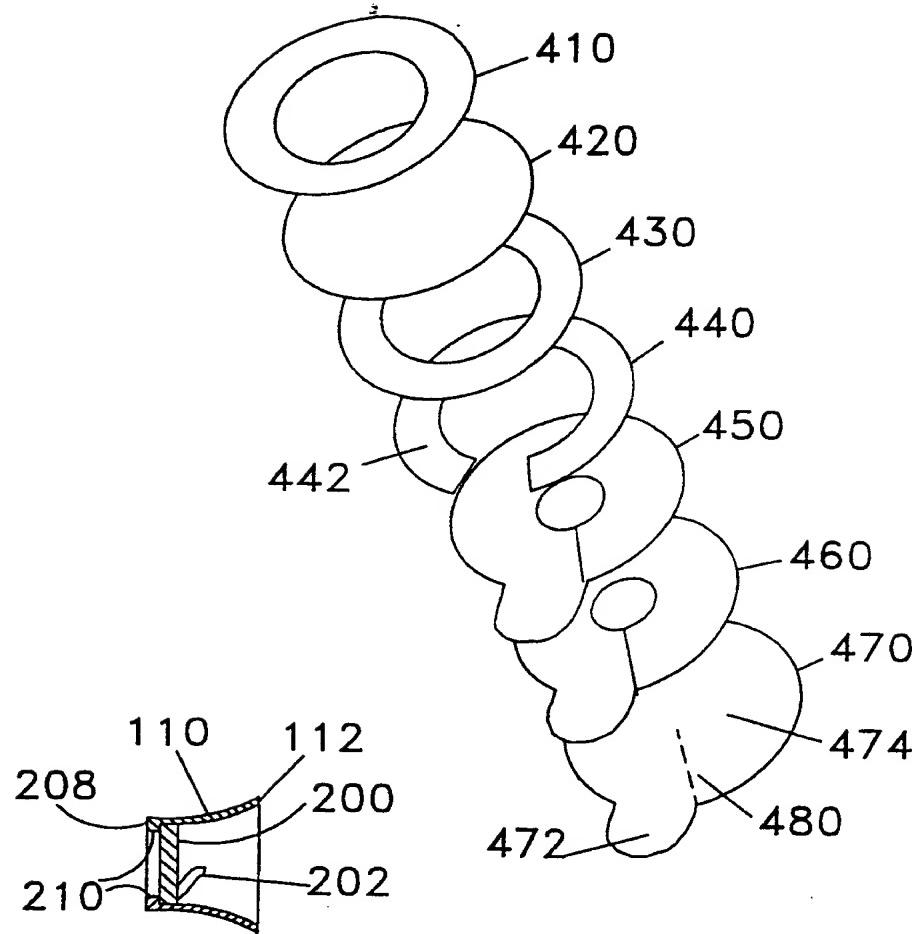
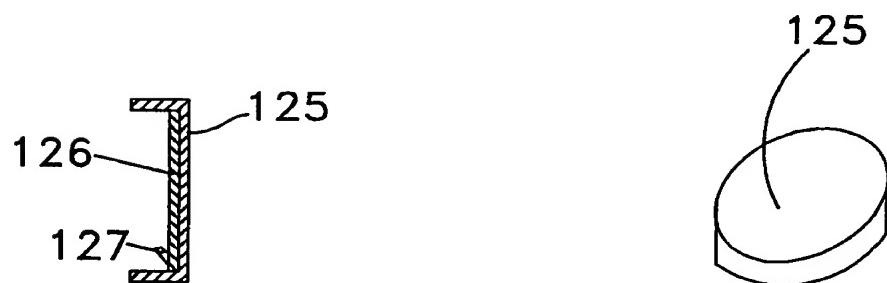


FIG. 14



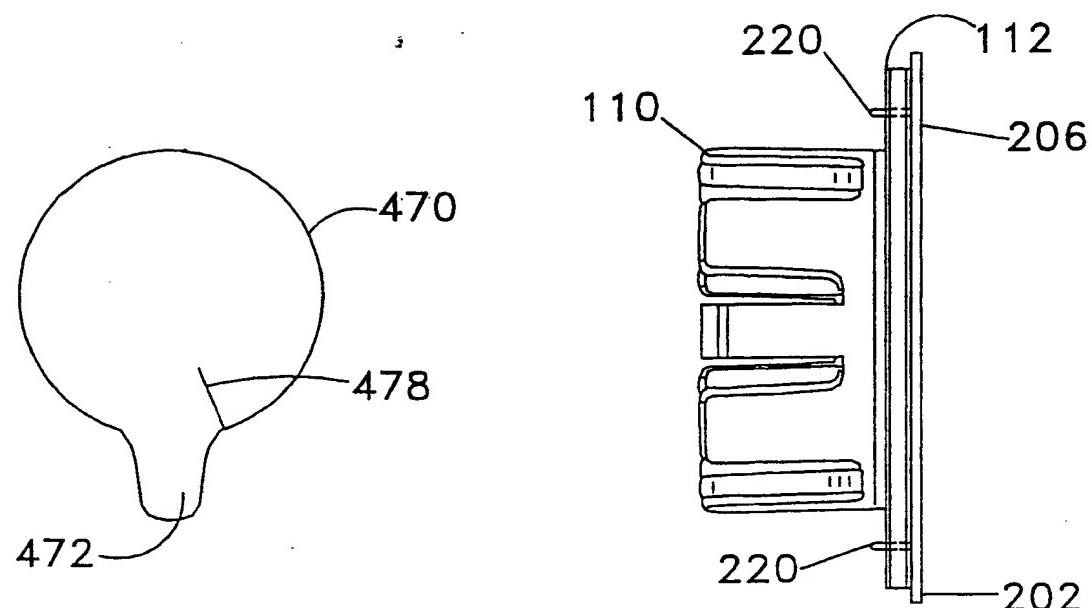


FIG. 16

FIG. 17

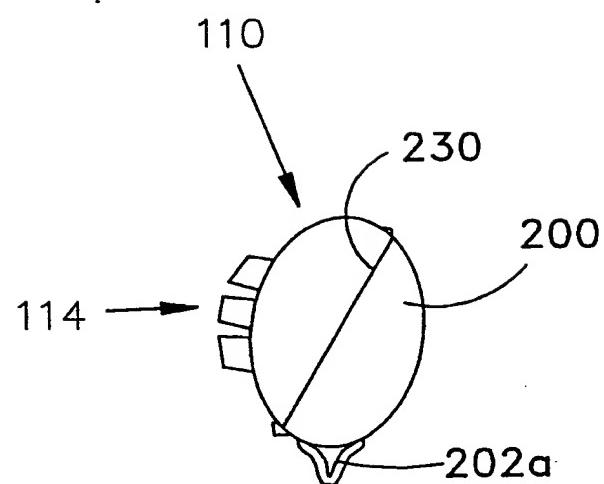


FIG. 18

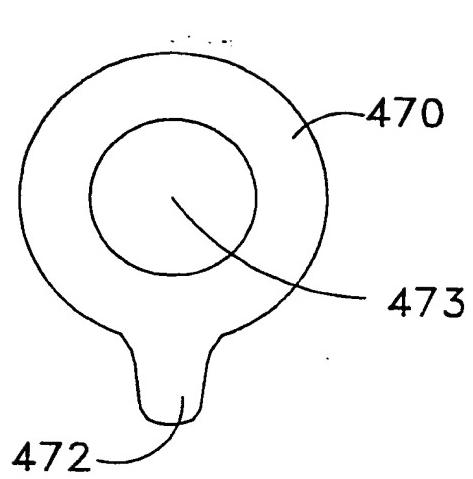


FIG. 19

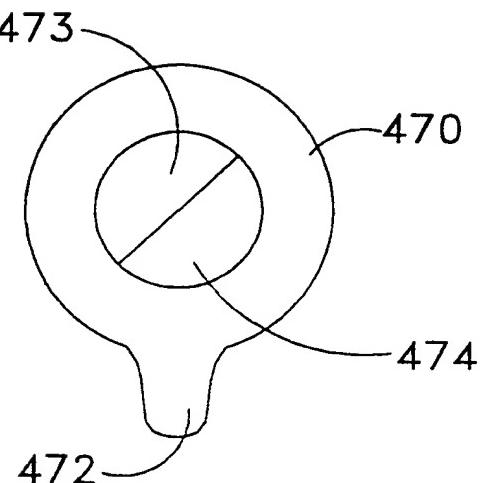


FIG. 20

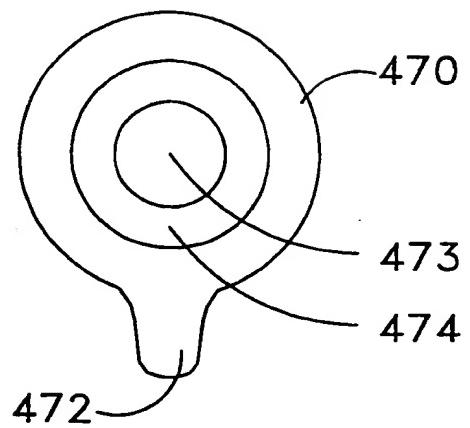
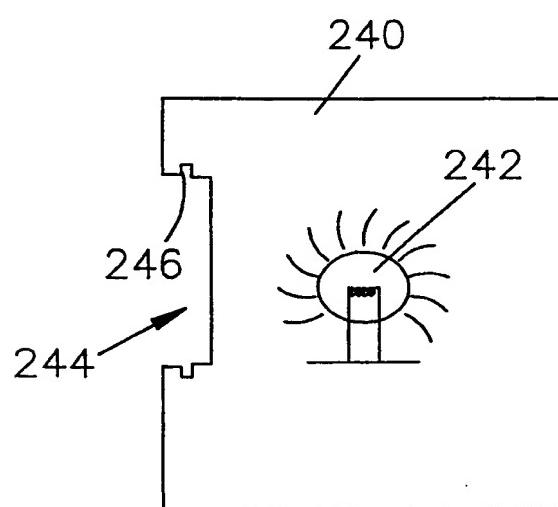
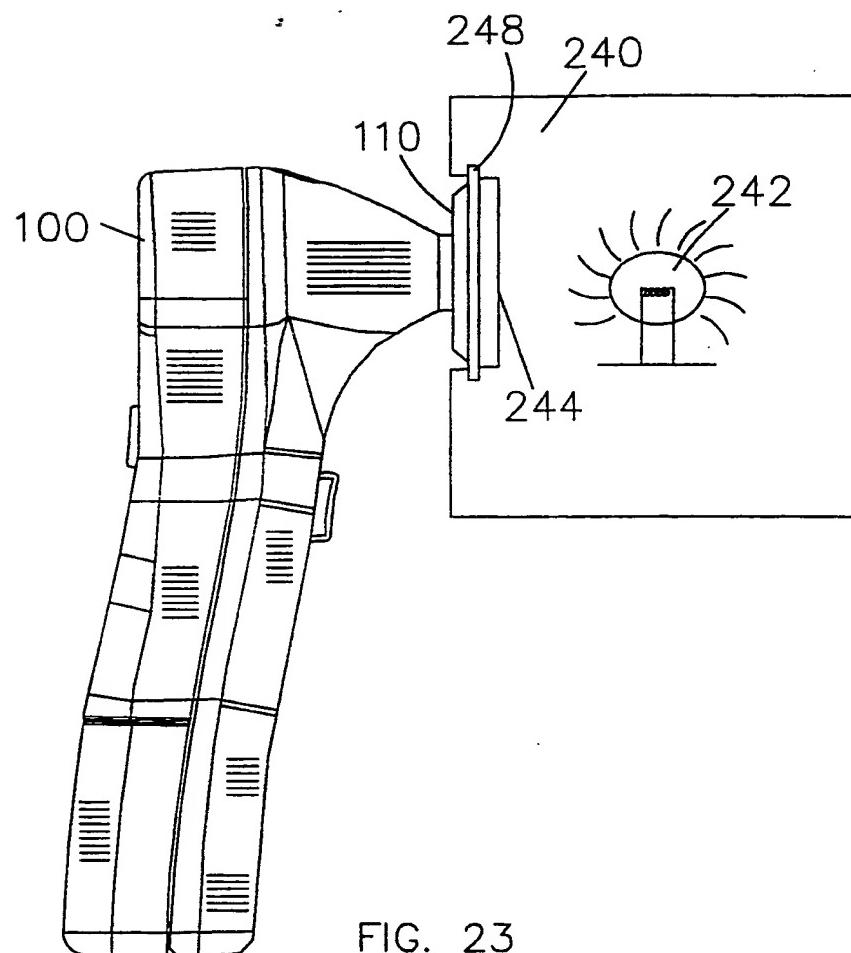


FIG. 21



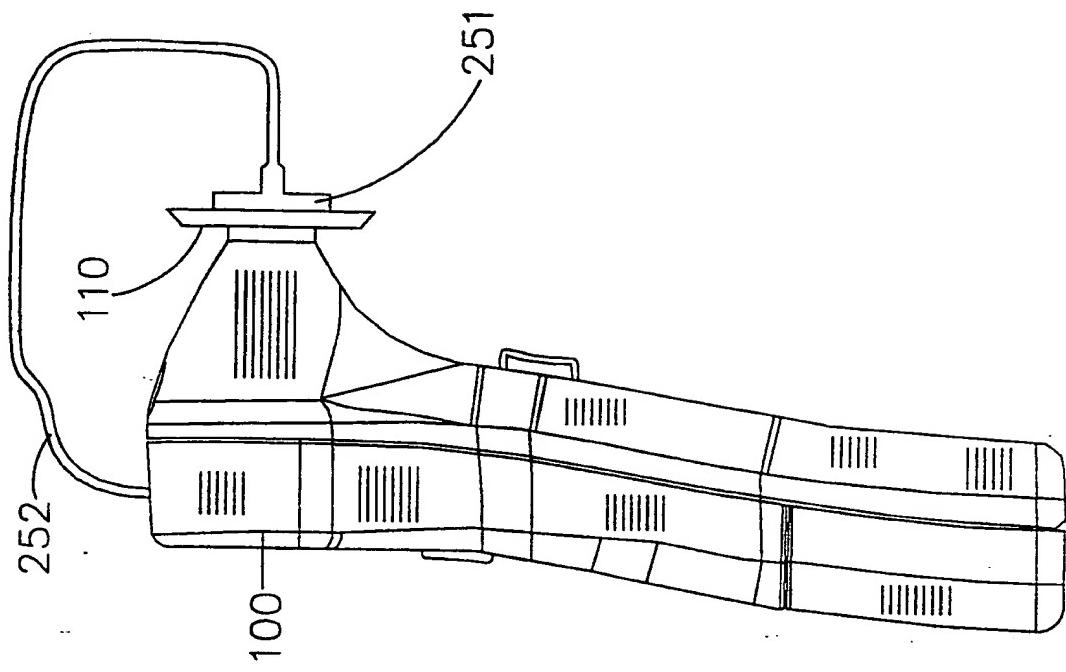


FIG. 24B

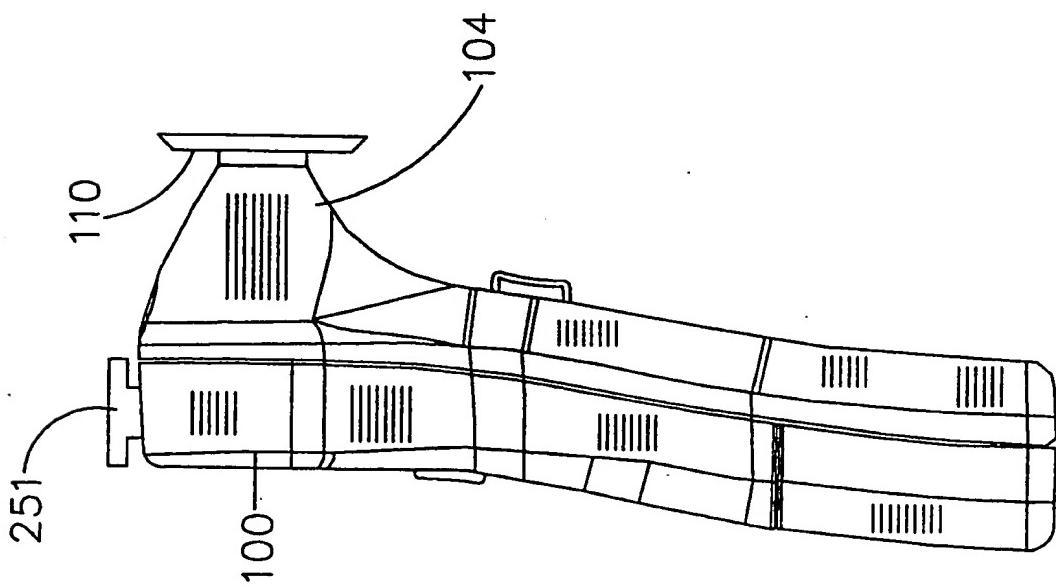


FIG. 24A

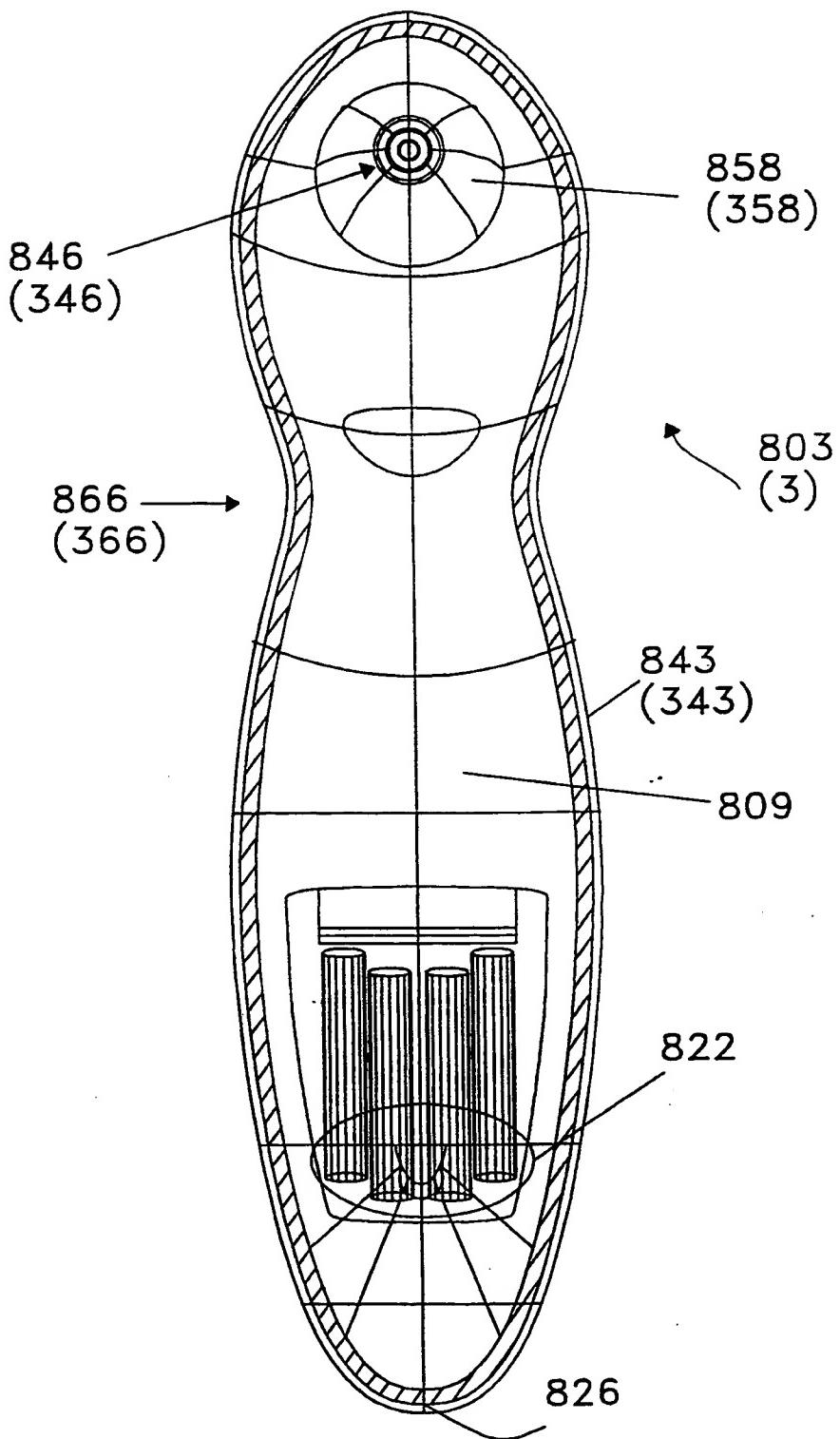


FIG. 25A

SUBSTITUTE SHEET (RULE 26)

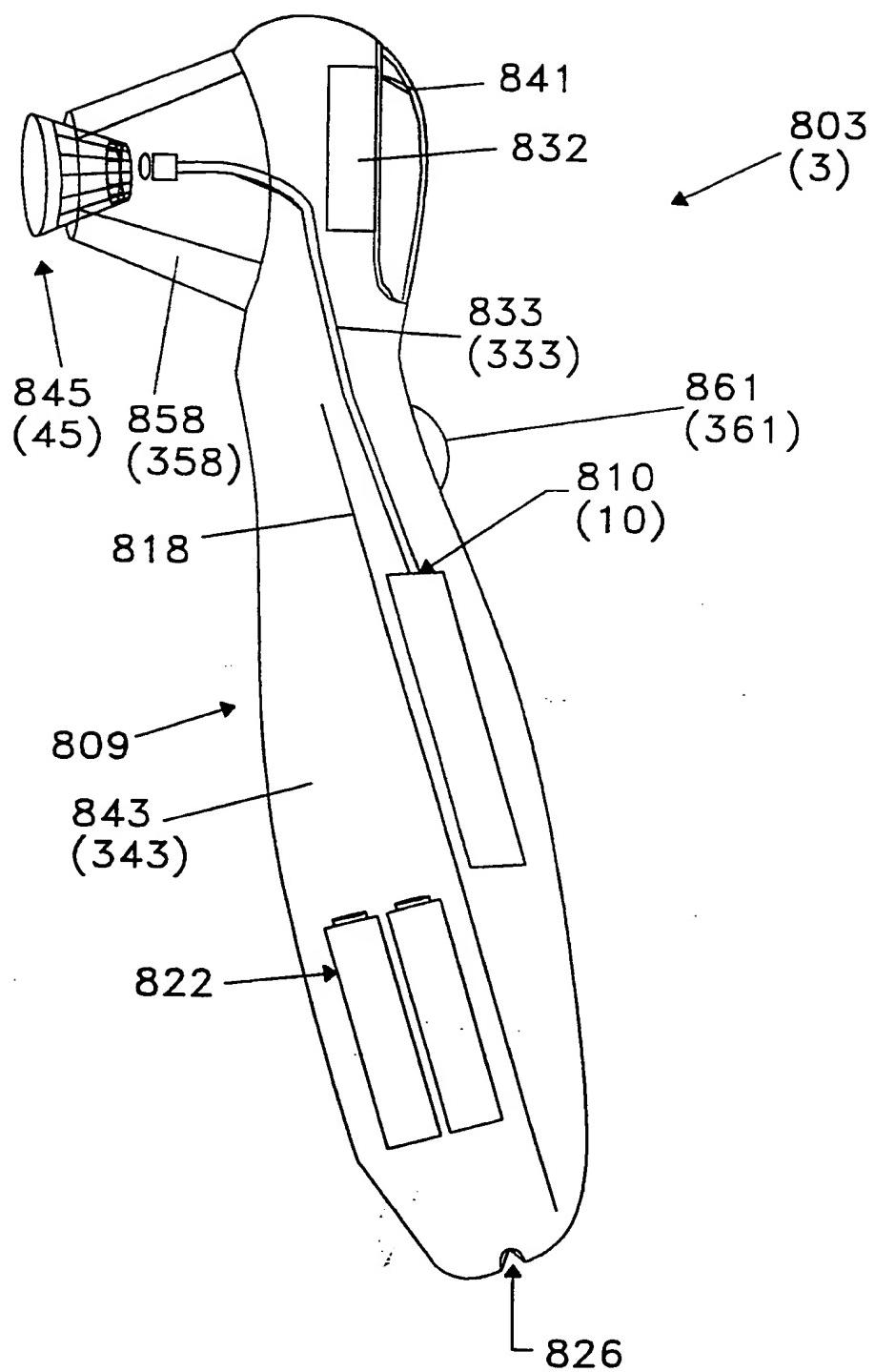


FIG. 25B

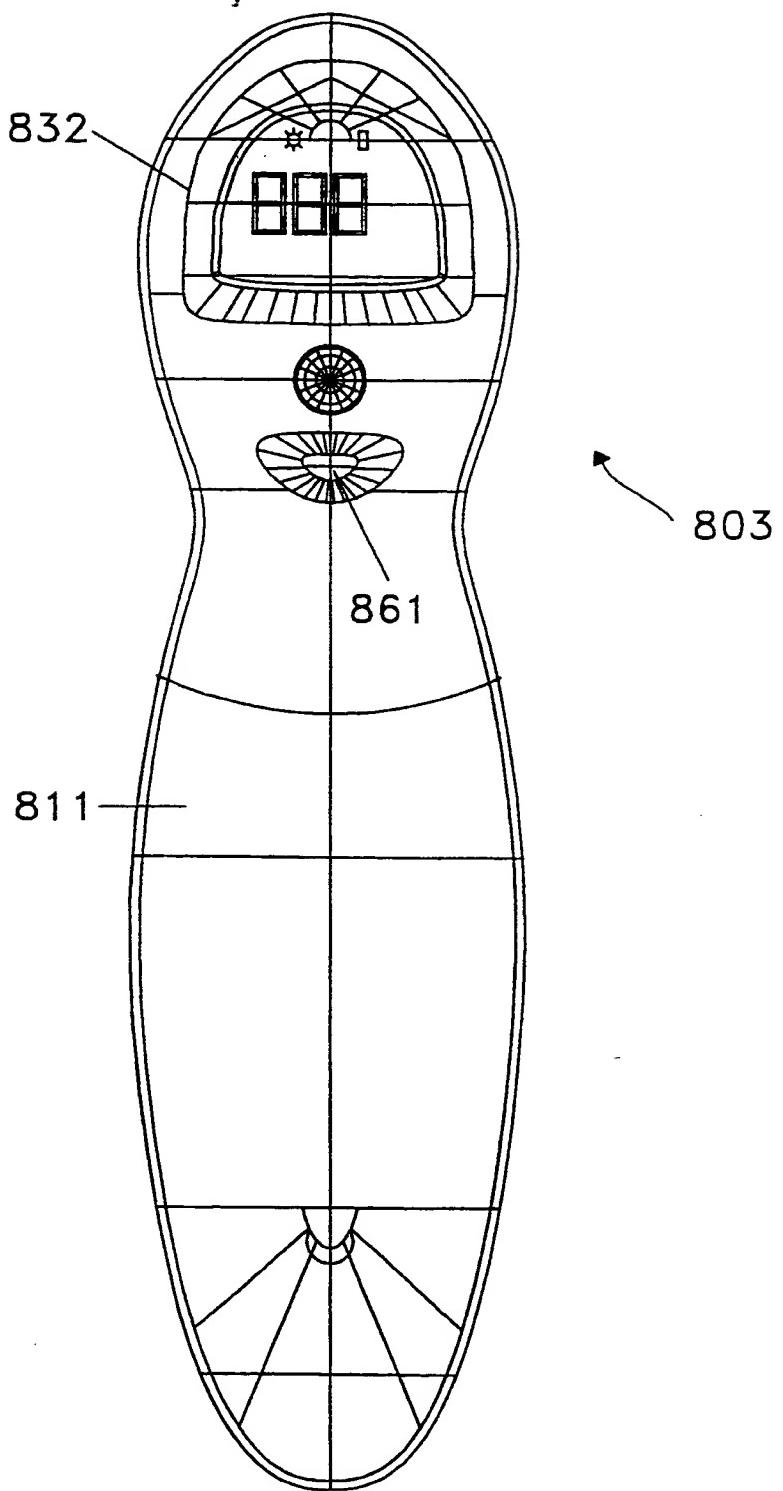


FIG. 25C

SUBSTITUTE SHEET (RULE 26)

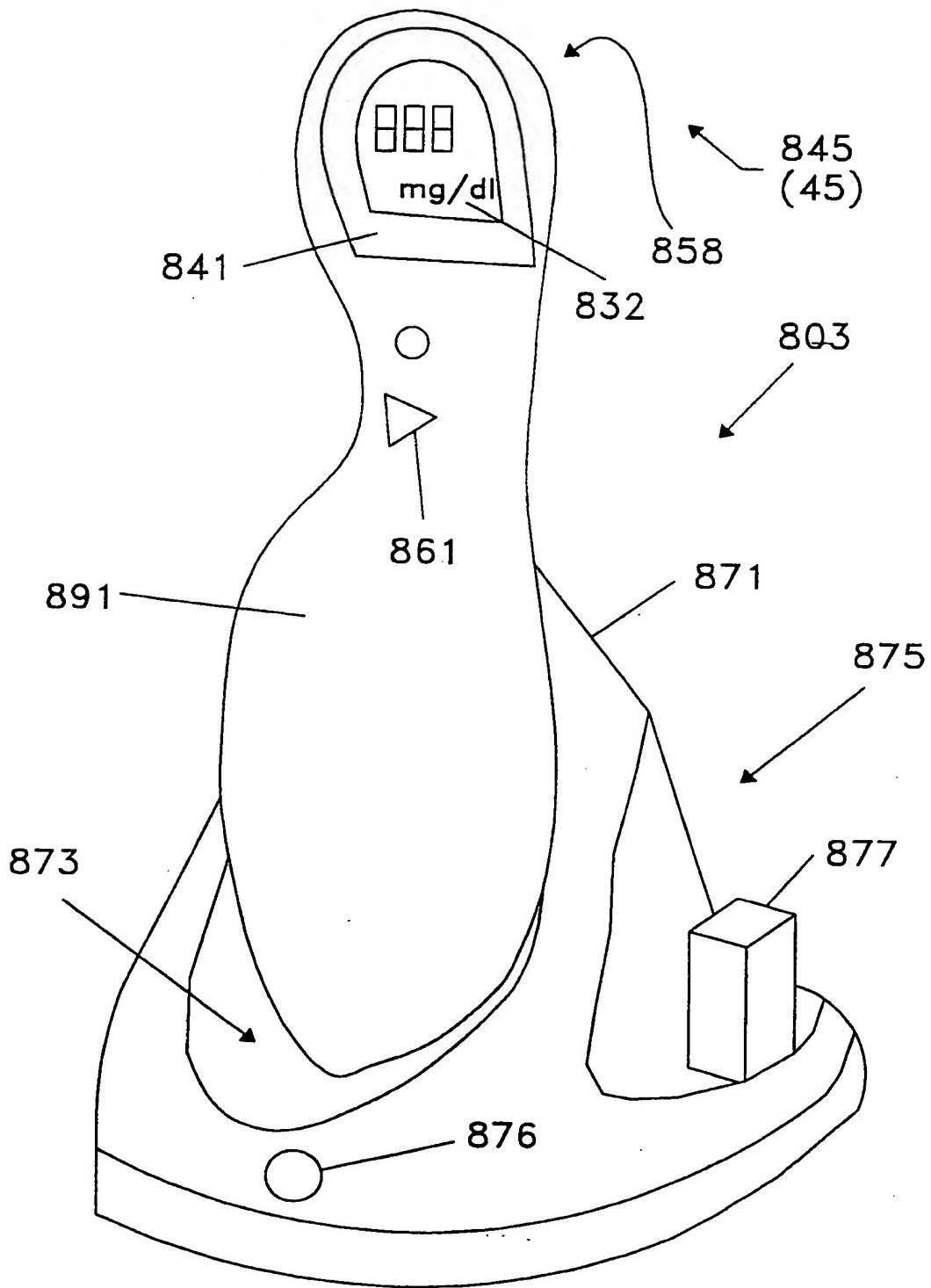


FIG. 25D

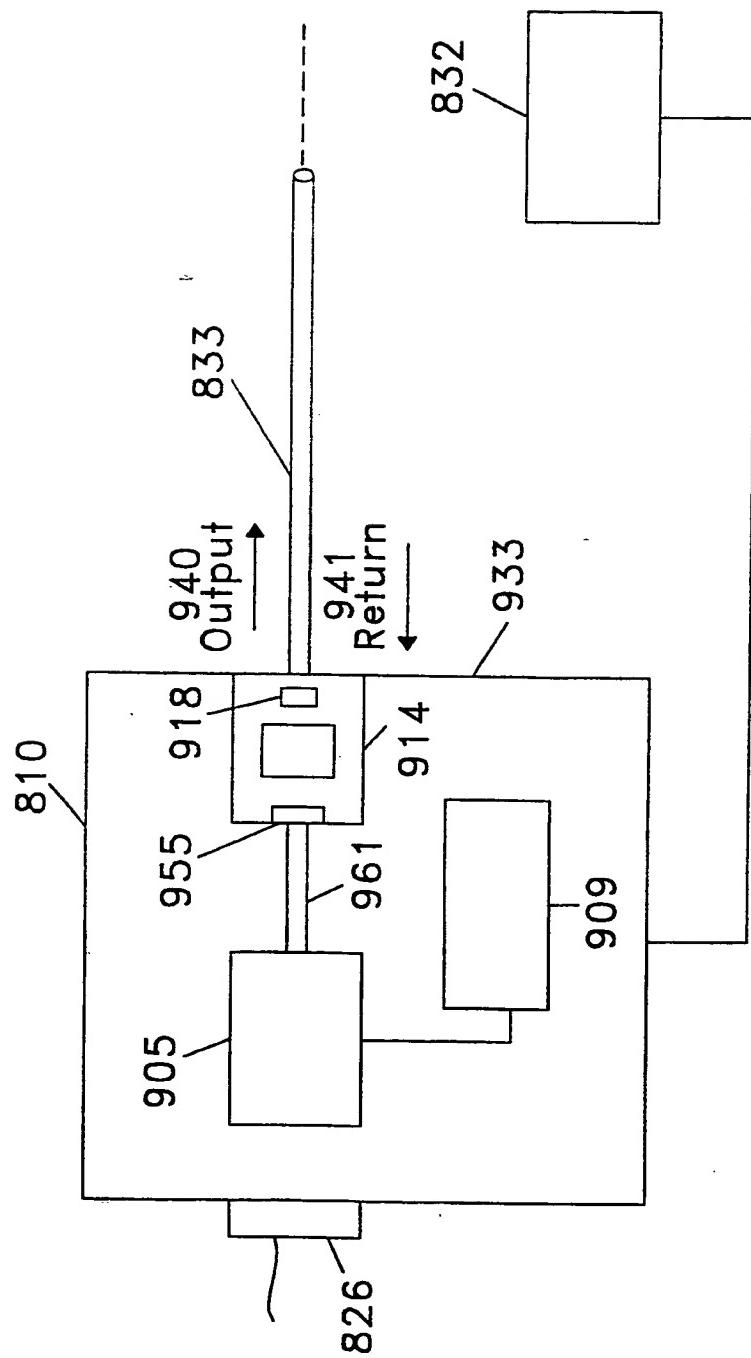


FIG. 26A

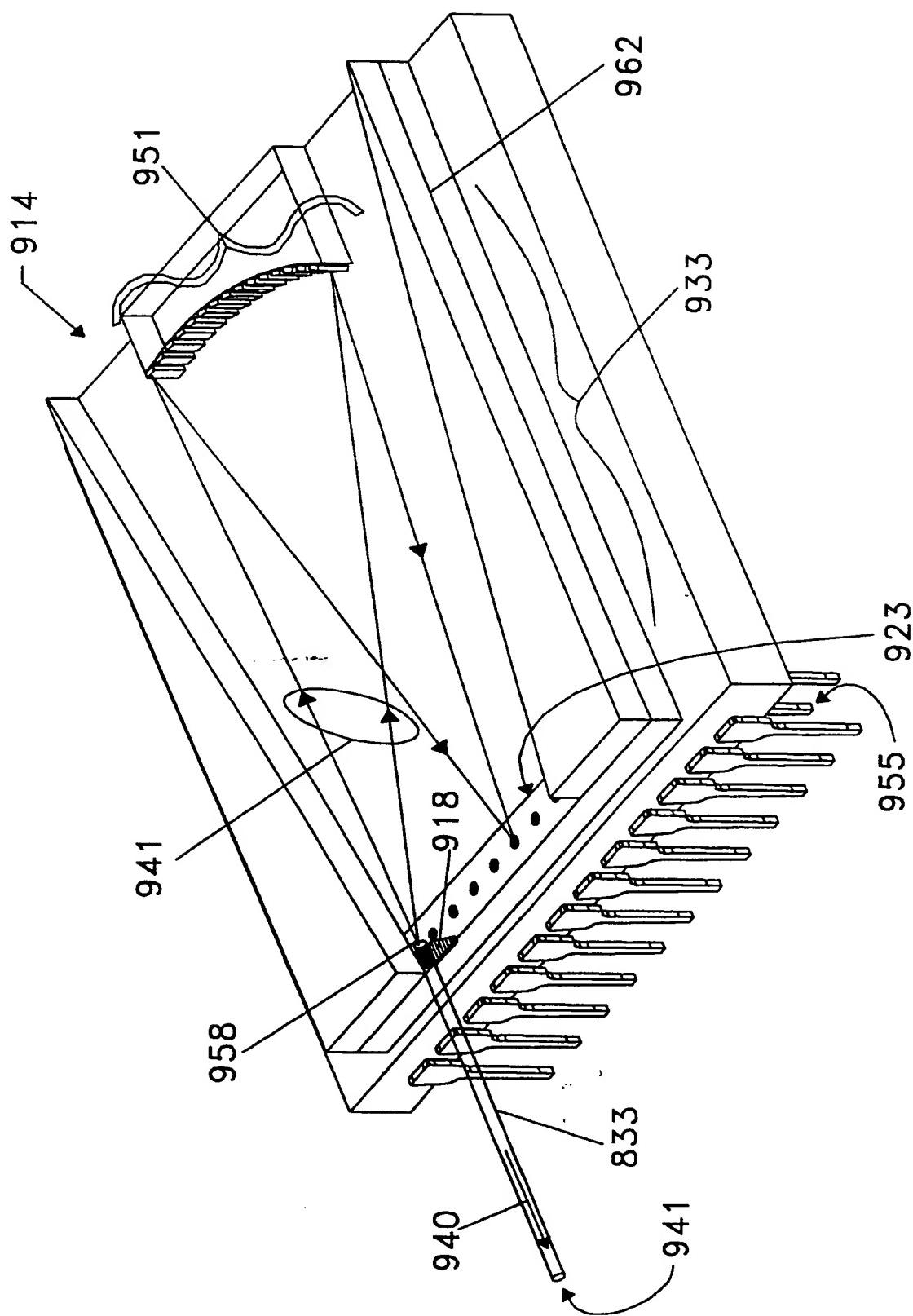


FIG. 26B

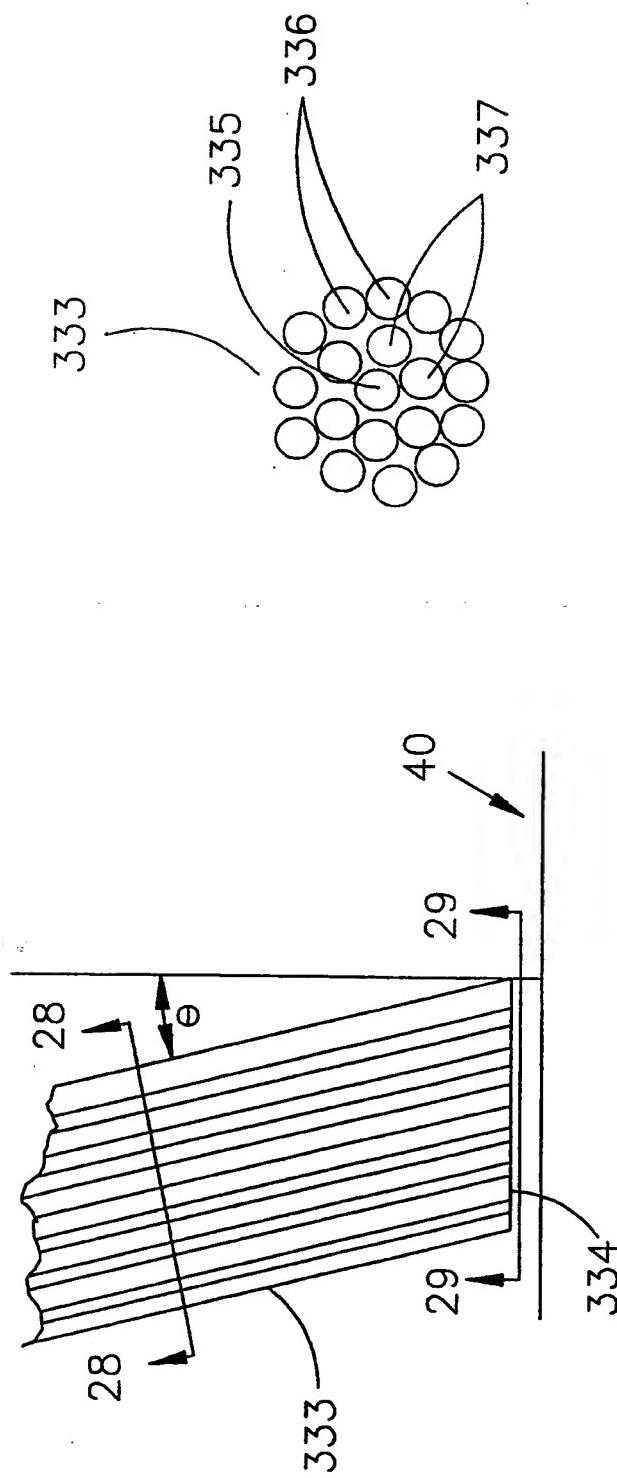


FIG. 27
FIG. 28

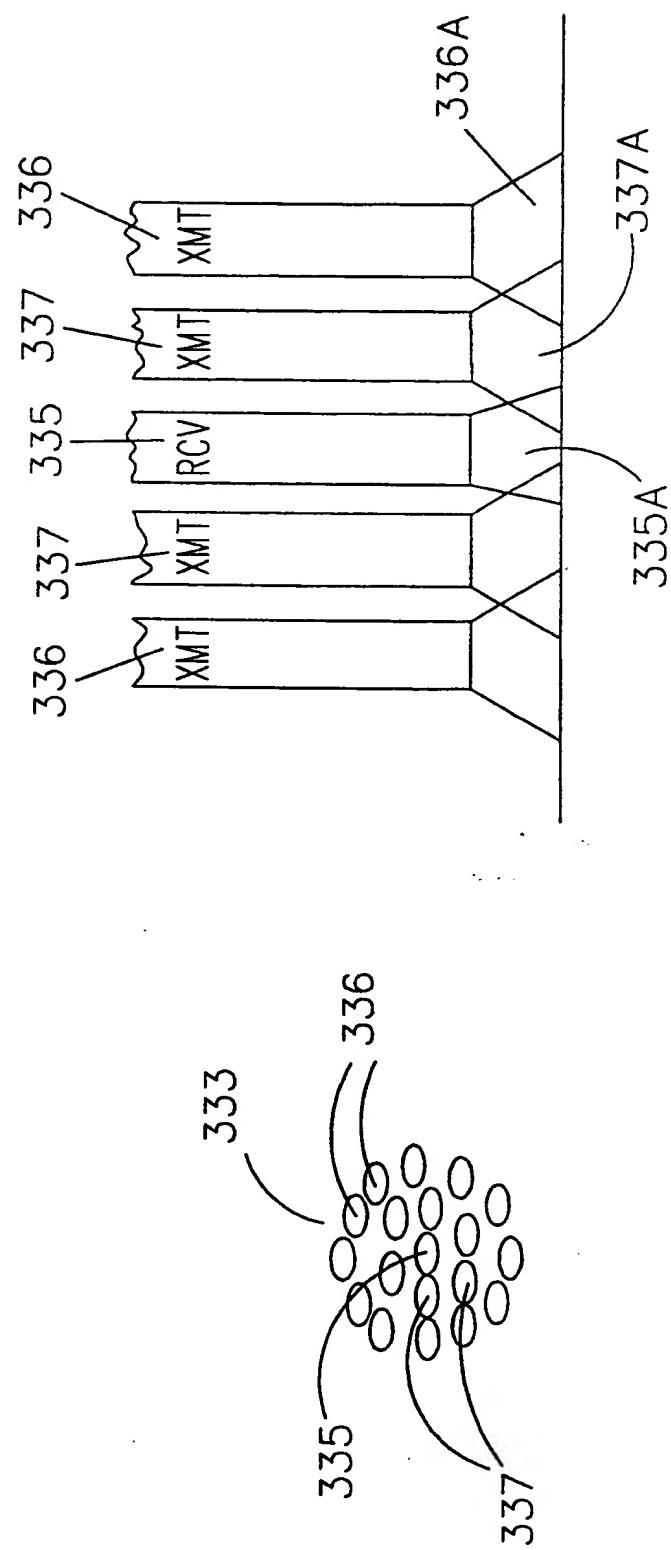


FIG. 29

FIG. 30

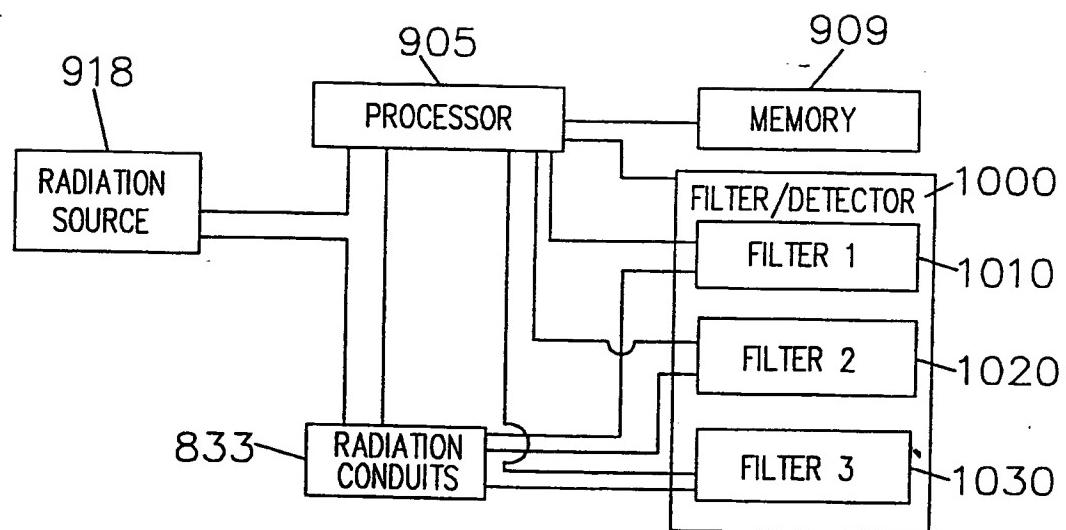


FIG. 31

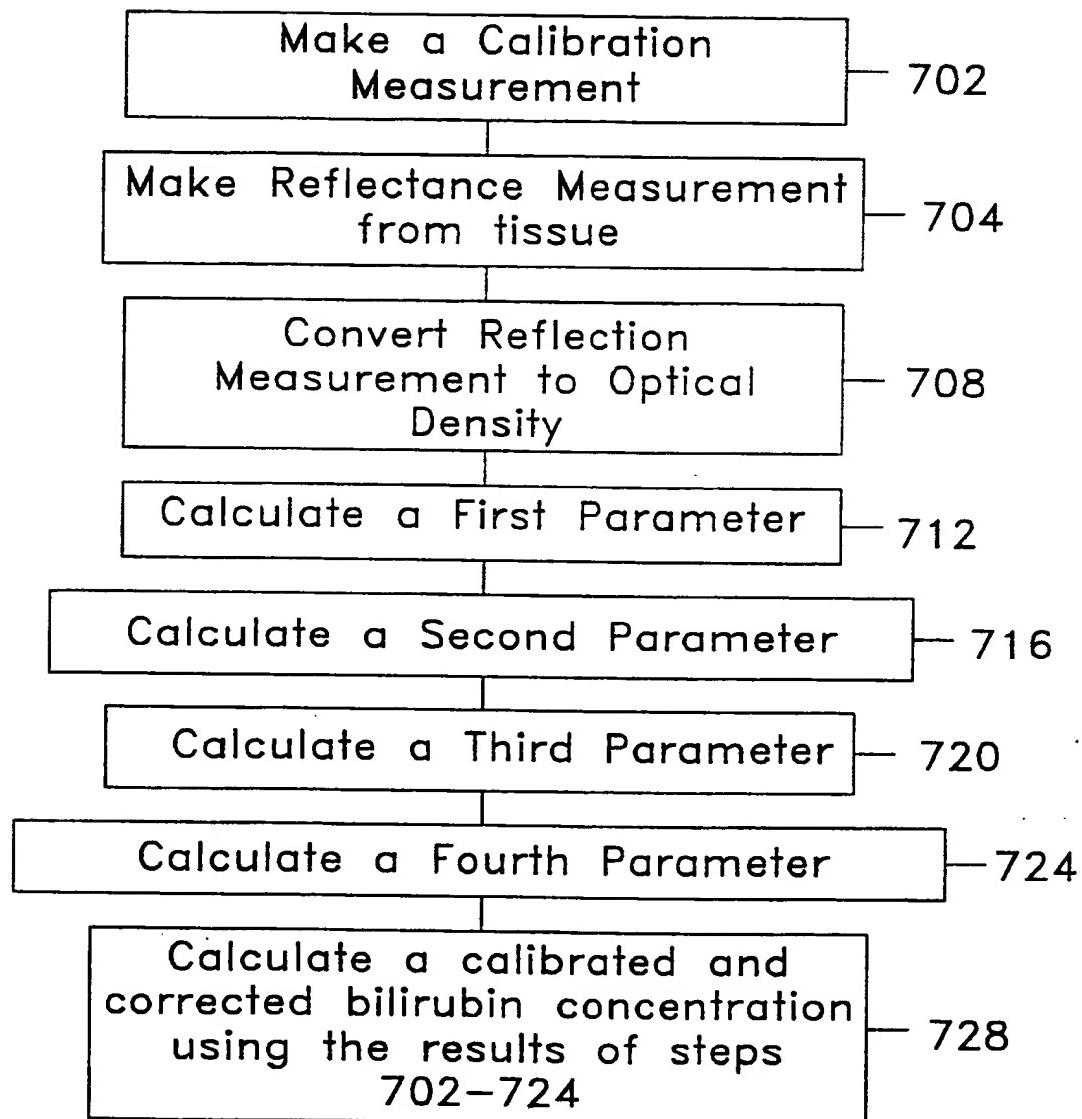


FIG. 32

Median Probe A Biliscore—vs—Serum
Bilirubin, Cln Site A, GJN, 13-Mar-96

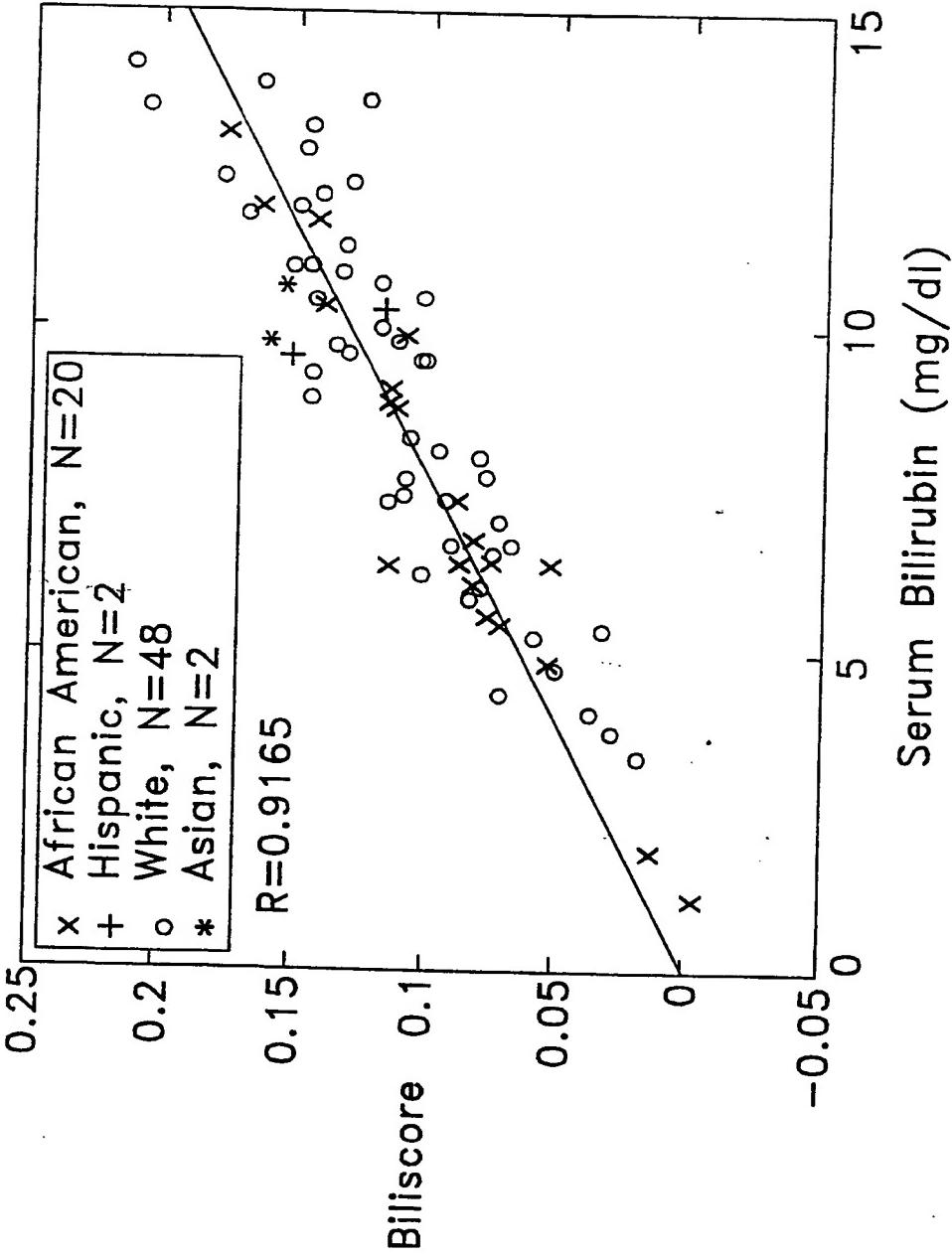


FIG. 33

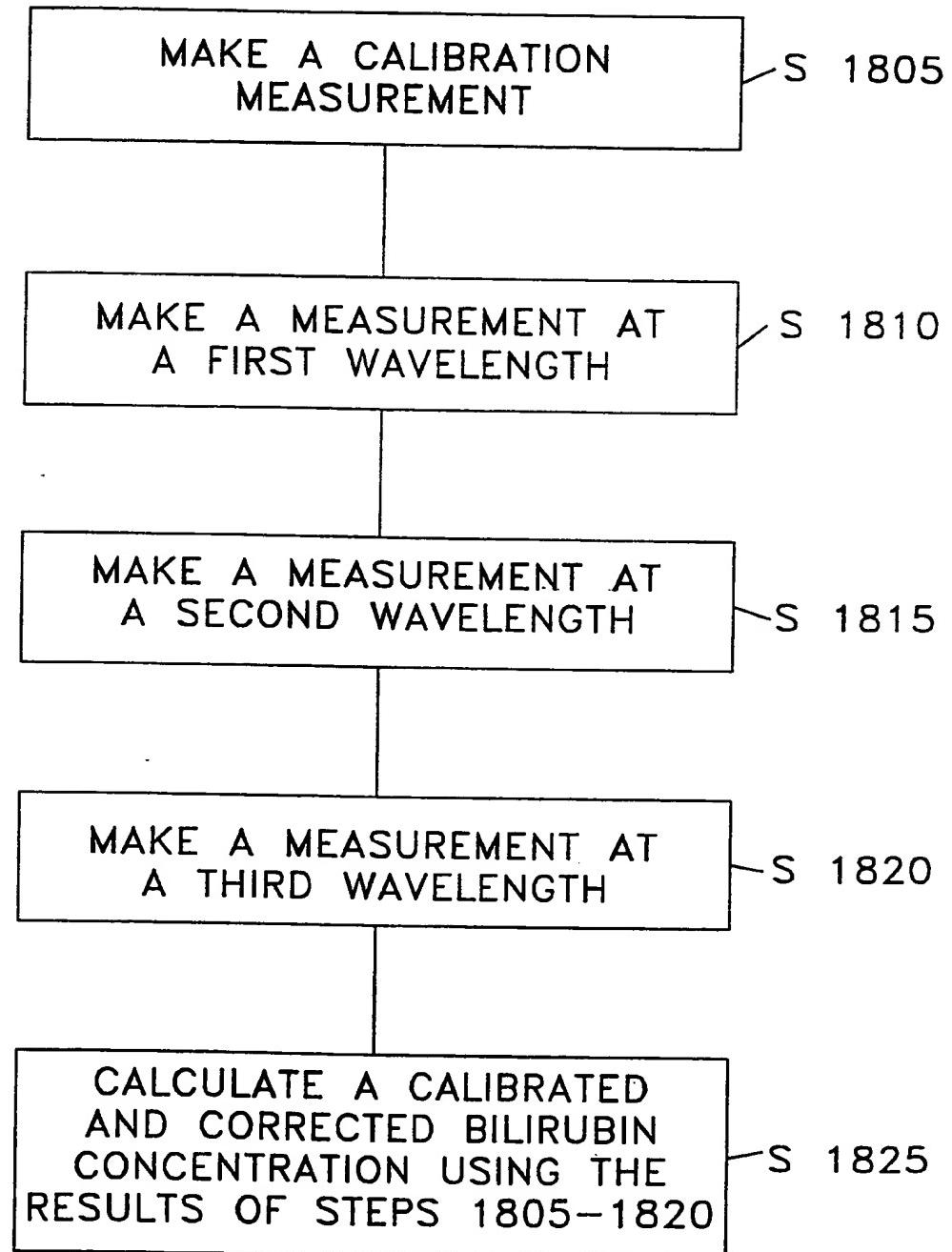


FIG. 34

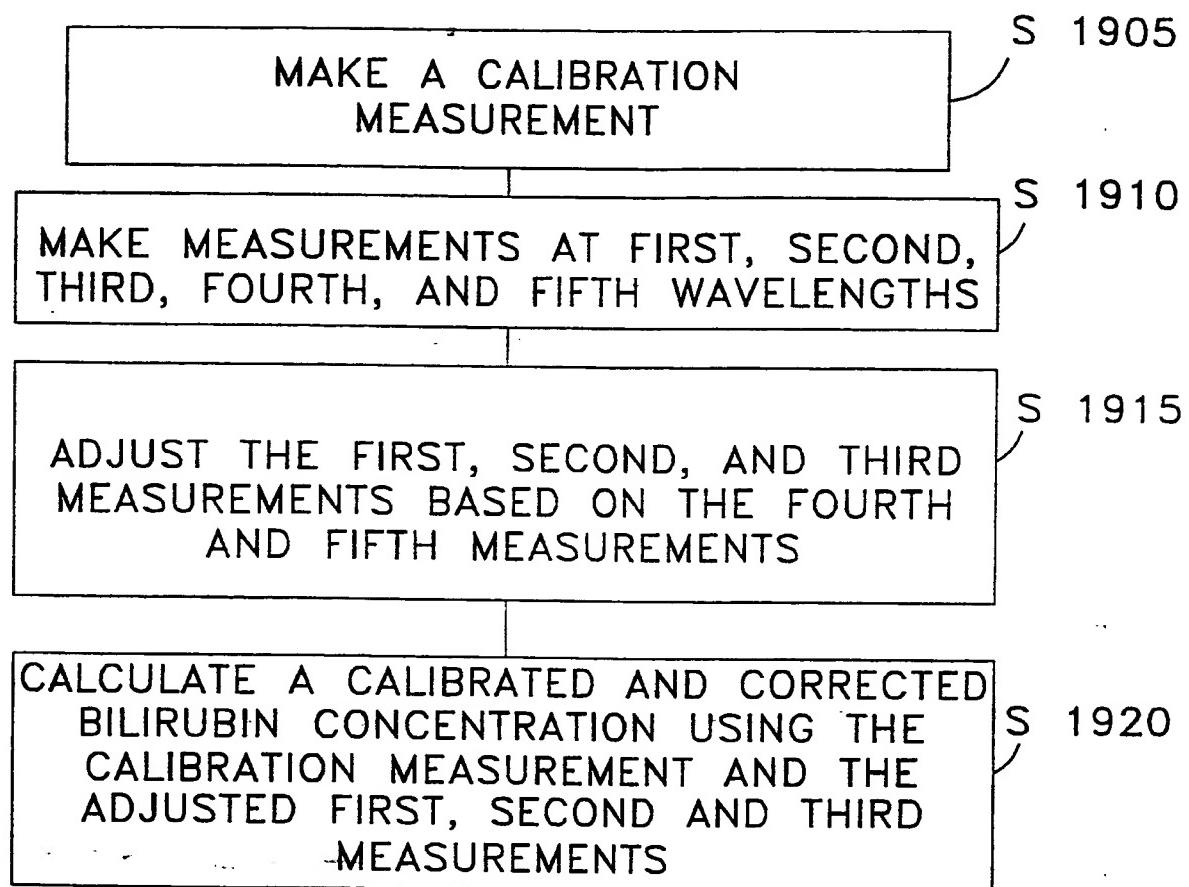


FIG. 37

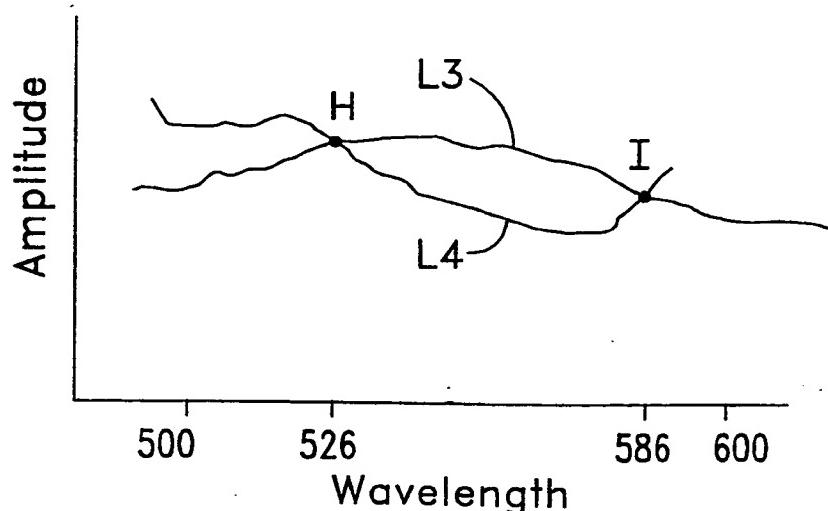


FIG. 35

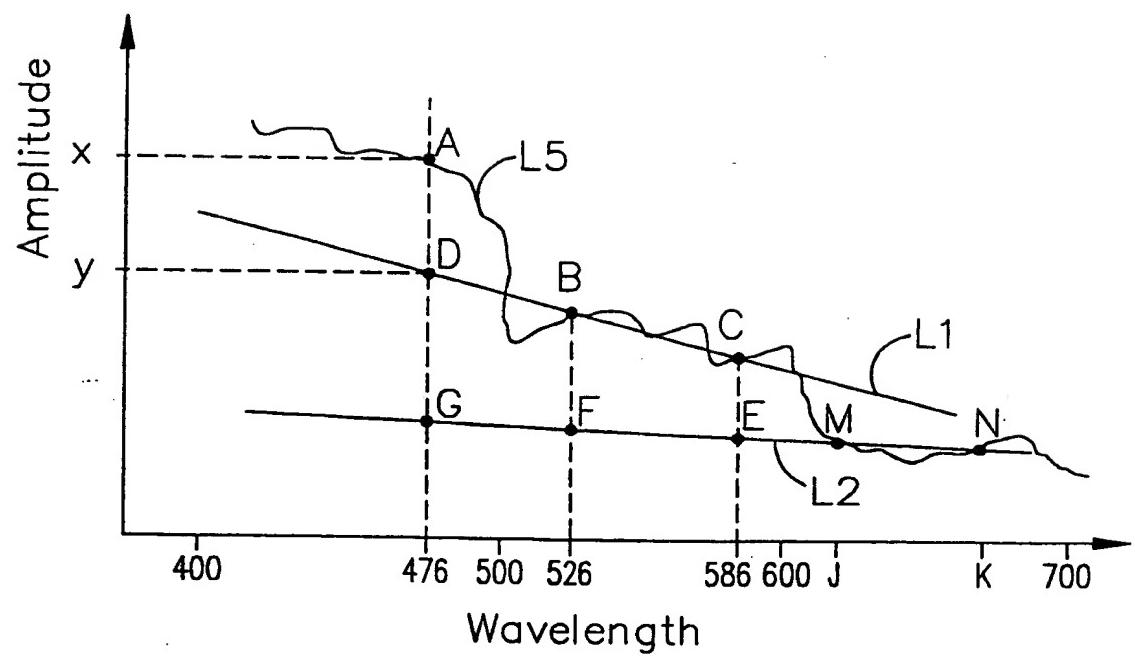


FIG. 36

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/15597

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 5/00
US CL :600/306

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 73/620, 621; 250/491.1; 355/20, 81; 356/243, 244; 367/140; 378/18, 207; 600/306, 309, 310, 442, 443, 473, 476

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	US 5,792,049 A (EPPSTEIN et al) 11 August 1998, entire document.	1-88

Further documents are listed in the continuation of Box C. See patent family annex.

A	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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P	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

03 SEPTEMBER 1998

Date of mailing of the international search report

28 SEP 1998

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